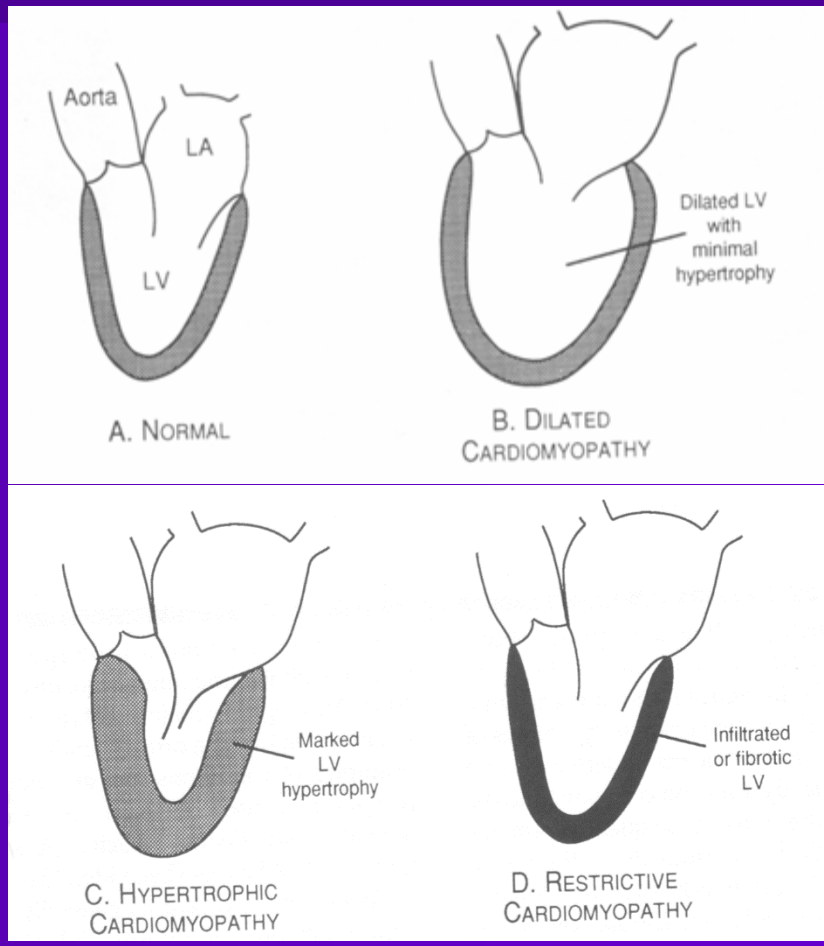
CARDIOMYOPATHIES

Cardiomyopathy

WHO Classification

anatomy & physiology of the LV

1. Dilated
   - Enlarged
   - Systolic dysfunction
2. Hypertrophic
   - Thickened
   - Diastolic dysfunction
3. Restrictive
   - Diastolic dysfunction
4. Arrhythmogenic RV dysplasia
   - Fibrofatty replacement
5. Unclassified
   - Fibroelastosis
   - LV noncompaction



CM: Specific Etiologies

- Ischemic
- Valvular
- Hypertensive
- Inflammatory
- Metabolic
- Inherited
- Toxic reactions
- Peripartum

Ischemic: thinned, scarred tissue

Dilated Cardiomyopathy

- Big, baggy heart- 'low EF%'
  - - Ischaemic (Coronary artery disease (plumbing))
  - -Burnt out hypertension
  - - Familial /inherited
  - - Alcohol cardiomyopathy
  - - Post viral (myocarditis)
  - - Unknown (idiopathic)
  - - Pregnancy related (peripartum)
  - - due to rhythm disturbance (tachycardia mediated)
  - - due to severe heart valve problem
  - - due to chemotherapy or radiotherapy
  - - dysynchrony

Dilated Cardiomyopathy

- Dilation *and* impaired contraction of ventricles:
  - Reduced *systolic* function with or without heart failure
  - Characterized by myocyte damage
  - Multiple etiologies with similar resultant pathophysiology

- Majority of cases are **idiopathic**
  - incidence of idiopathic dilated CM 5-8/100,000
  - incidence likely higher due to mild, asymptomatic cases
  - 3X more prevalent among males and African-Americans

DCM: Etiology

Ischemic

Valvular

Hypertensive

Familial

Idiopathic

Inflammatory

- **Infectious**
  - **Viral – picornovirus, Cox B, CMV, HIV**
  - **Ricketsial - Lyme Disease**
  - **Parasitic - Chagas' Disease, Toxoplasmosis**
- **Non-infectious**
  - **Collagen Vascular Disease (SLE, RA)**
  - **Peripartum**

Toxic

- **Alcohol, Anthracyclins (adriamycin), Cocaine**

Metabolic

- **Endocrine –thyroid dz, pheochromocytoma, DM, acromegaly,**

Nutritional

- **Thiamine, selenium, carnitine**

Neuromuscular (Duchene's Muscular Dystrophy--x-linked)

DCM: Infectious

Acute viral myocarditis

- Coxasackie B or echovirus
- Self-limited infection in young people
- Mechanism?:
  - Myocyte cell death and fibrosis
  - Immune mediated injury
  - BUT:
    - No change with immunosuppressive drugs

DCM: toxic

Alcoholic cardiomyopathy

- Chronic use
- Reversible with abstinence
- Mechanism?:
  - Myocyte cell death and fibrosis
  - Directly inhibits:
    - mitochondrial oxidative phosphorylation
    - Fatty acid oxidation

DCM: inherited

Familial cardiomyopathy

- 30% of 'idiopathic'
- Inheritance patterns
  - Autosommal dom/rec, x-linked, mitochondrial
- Associated phenotypes:
  - Skeletal muscle abn, neurologic, auditory
- Mechanism:
  - Abnormalities in:
    - Energy production
    - Contractile force generation
  - Specific genes coding for:
    - Myosin, actin, dystophin…

PERIPARTUM CARDIOMYOPATHY

- Peripartum cardiomyopathy is defined as the onset of acute heart failure without demonstrable cause in the last trimester of pregnancy or within the first 5 months after delivery.

Criteria for Peripartum Cardiomyopathy

1. Development of Cardiac failure in the last month of pregnancy or within 5 month after delivery
2. Absence of an identifiable cause for the cardiac failure.
3. Absence of recognizable heart disease prior to the last month of pregnancy.
4. Left ventricular systolic dysfunction demonstrated by classic Echo Cardio Graphic criteria such as depressed shortening fraction or ejection fraction.

The National Heart, Lung and Blood Institute and the Office of rare diseases (1997)

Etiology

Still unknown.

- -nutritional deficiencies
- -small vessel coronary artery abnormality
- -hormonal effects
- -toxemia
- -maternal immunologic response to fetal antigen or
- -myocarditis

Predisposing factors

- -maternal age greater than 30 yr
- -multiparous or eclamptic patients
- - twinning
- - racial origin (black)
- - hypertension and
- - nutritional deficiencies
- In majority of cases there is no family history

Symptoms

Symptoms of worsening cardiac failure like:

- -dyspnoea on exertion
- -fatigue
- -ankle oedema
- -embolic phenomena
- -atypical chest pains and
- -haemoptysis.
- Many of above symptoms may occur even in normal pregnancy and can be mistaken for a diseased state.

Signs

- -evidence of a raised CVP
- -tachycardia
- -cardiomegaly with a gallop rhythm (S3)
- -mitral regurgitation
- -pulmonary crackles and
- -peripheral oedema.

PERIPARTUM CARDIOMYOPATHY

Chest radiograph:

- cardiomegaly with pulmonary oedema
- pulmonary venous congestion.

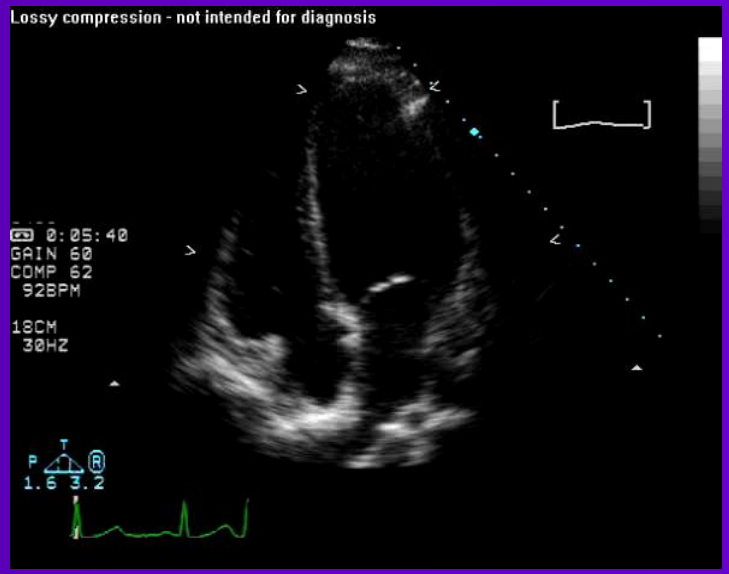
The ElectroCardioGram:

- nonspecific ST and T wave changes
- atrial or ventricular arrhythmias and
- conduction defects.

DCM: Peripartum

Diagnostic Criteria

- 1 mo pre, 5 mos post
- Echo: LV dysfunction
  - LVEF < 45%
  - LVEDD > 2.7 cm/m2
- Epidemiology/Etiology
- 1:4000 women
    - JAMA 2000;283:1183
- Proposed mechanisms:
  - Inflammatory Cytokines:
    - TNFa, IL6, Fas/AP01
      - JACC 2000 35(3):701.



Echocardiography / Doppler

- may reveal enlargement of all four chambers with marked reduction in left ventricular systolic function
- small to moderate pericardial effusion and
- mitral, tricuspid and pulmonary regurgitation
- Ventricular wall motion, ejection fraction and cardiac output are

PPCM: Prognosis

- Death from CM: ’91-97
  - 245 CM deaths in US, 0.88/100,000 live births, 70% peripartum
  - Increased risk with:
    - Maternal age
    - AA 6.4x greater
      - Whitehead SJ. ObGyn2003;102:1326.
- Risk of recurrent pregnancy
  - Retrospective survey : 44 women (16 vs 28)
    - Reduced EF, CHF 44% vs 21%, mortality 0 vs. 19%
      - Elkyam U. NEJM.2001;344:1567.
  - DSE:contractile reserve reduced in patients
    - 7 women: change in Vcf_c σ_{ES} relationship
      - Lampert MB. AJOG.1997.176.189.

Dilated Cardiomyopathy

MECHANISMS IN HEART FAILURE

Ischemic injury
Myocardial disease
Genetics

Neurohormones
Cytokines
Oxidative stress

Altered molecular expression
Ultrastructural changes
Myocyte hypertrophy
Myocyte contractile dysfunction
Apoptosis
Fibroblast proliferation
Collagen deposition
Ventricular remodeling

Hemodynamic Derangement
Clinical Heart Failure
Arrhythmia

Pathophysiology

- Initial Compensation for impaired myocyte contractility:
  - Frank-Starling mechanism
  - Neurohumoral activation
  - ↑ intravascular volume
- Eventual decompensation
  - ventricular remodeling
  - myocyte death/apoptosis
  - valvular regurgitation

Pathophysiology: Starling Curve

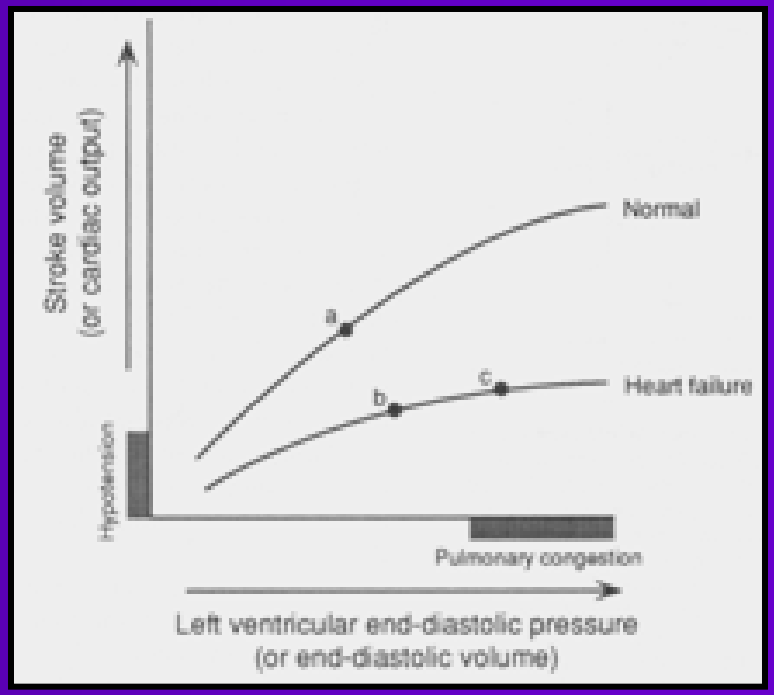
PRELOAD =
END-DIASTOLIC
MYOCARDIAL FIBER
STRETCH

LV STROKE WORK

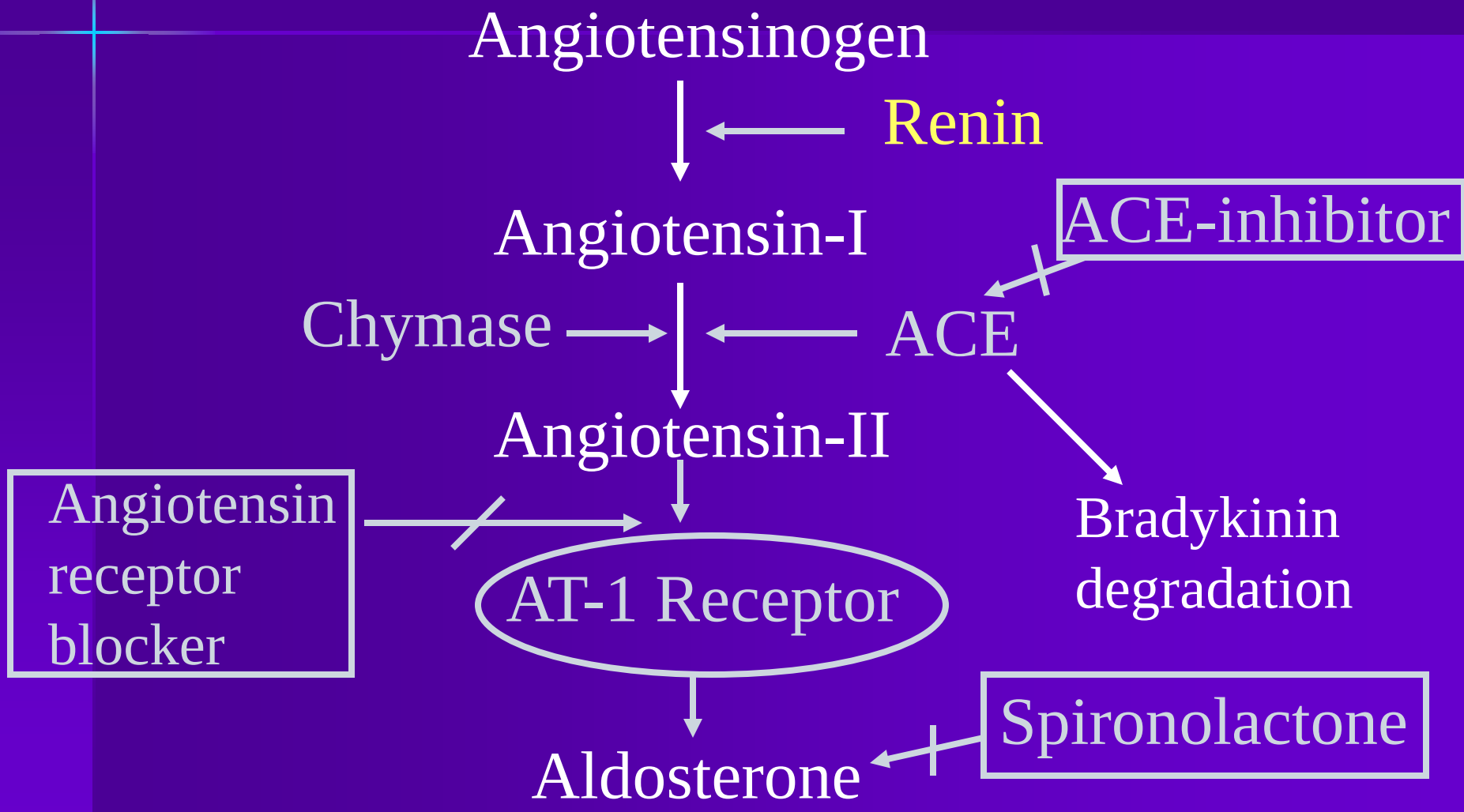
=STROKE VOLUME
x GENERATED
PRESSURE

END-DIASTOLIC FIBER STRETCH
DIMENSION
VOLUME
PRESSURE

LEFT ATRIAL PRESSURE
PULM VEN PRESSURE
PA WEDGE PRESSURE



Renin-Angiotensin-Aldosterone Pathways



Angiotensin-II Effects

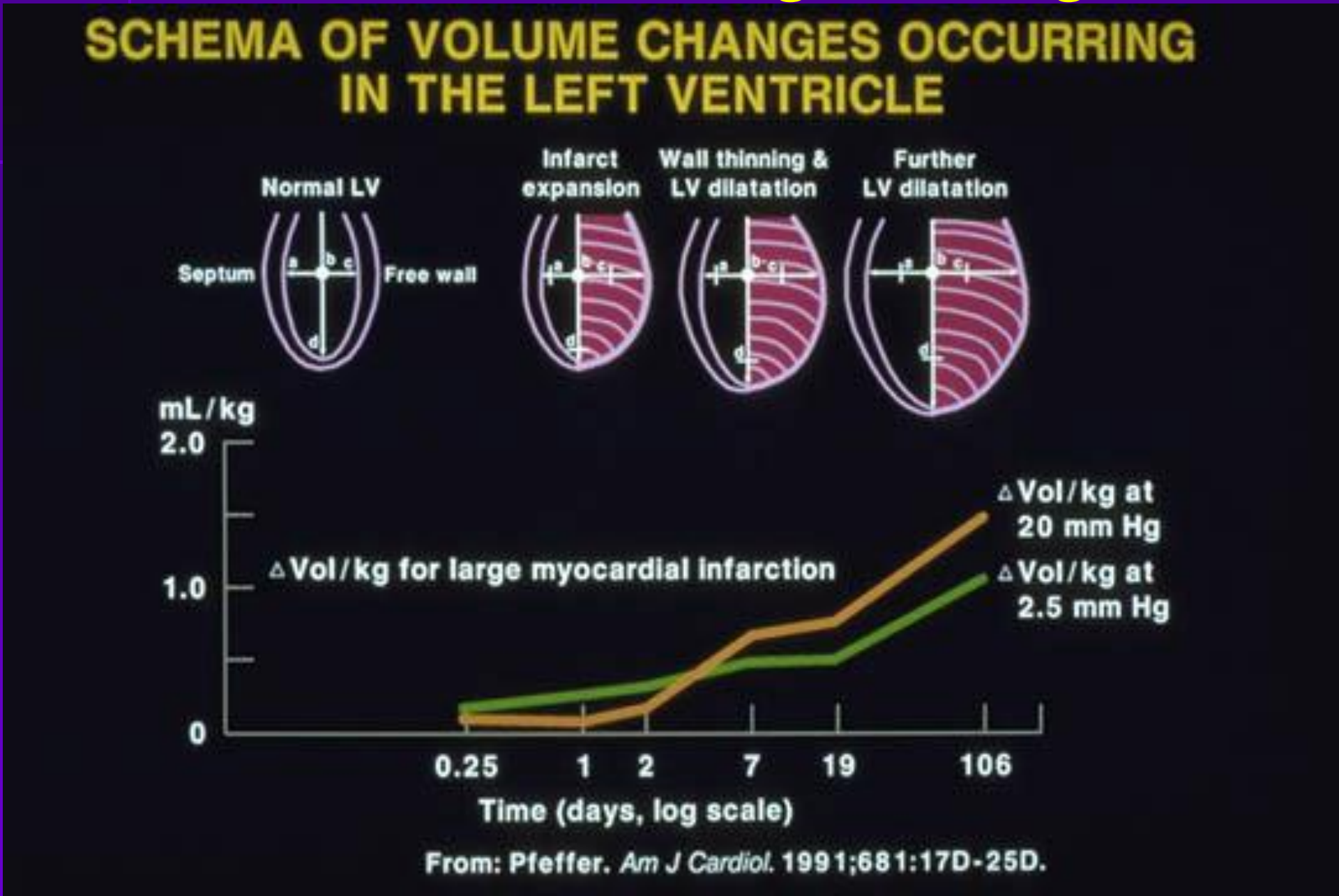
- Vasoconstriction
- Aldosterone production
- Myocyte hypertrophy
- Fibroblast proliferation
- Collagen deposition
- Apoptosis
- Pro-thrombotic
- Pro-oxidant
- Adrenergic stimulation
- Endothelial dysfunction

The Kidney in Heart Failure

- Reduced renal blood flow
- Reduced glomerular filtration rate
- Increased renin production
- Increased tubular sodium reabsorption
- Increased free water retention (vasopressin)

Ventricular Remodeling in Heart Failure

Ventricular Remodeling following MI



Extracellular Stimuli of Myocyte Hypertrophy

Type	**Examples**
Mechanical	Stretch
Vasoactive peptides	Angiotensin-II Endothelin-1
α–adrenergic agonists	Norepinephrine
Peptide growth factors	Fibroblast GF Insulin-like GF
Cytokines	TNF-α

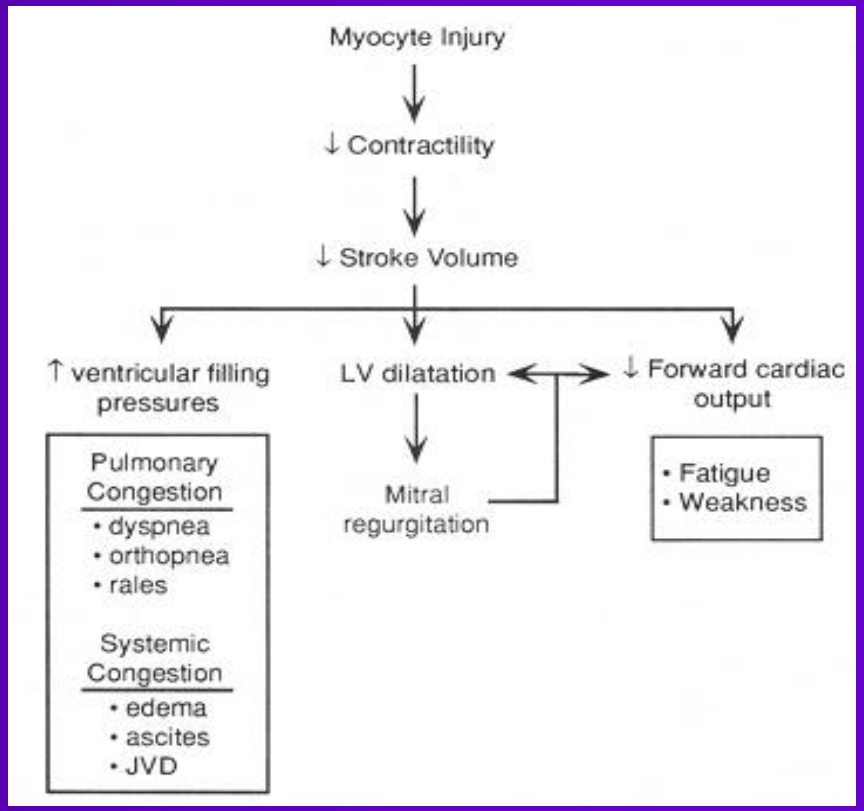
Clinical Findings

Biventricular Congestive Heart Failure

-Low forward Cardiac Output
-fatigue, lightheadedness, hypotension

-Pulmonary Congestion
-Dyspnea,
-orthopnea, & PND

-Systemic Congestion
-Edema
-Ascites
-Weight gain



Physical Exam

- Decreased C.O.
  - Tachycardia
  - ↓ BP and pulse pressure
  - cool extremities (vasoconstriction)
  - Pulsus Alternans (end-stage)
- Pulmonary venous congestion:
  - rales
  - pleural effusions
- Cardiac:
  - laterally displaced PMI
  - S3 (acutely)
  - mitral regurgitation murmur
- Systemic congestion
  - ↑ JVD
  - hepatosplenomegaly
  - ascites
  - peripheral edema

Diagnostic Studies

CXR -enlarged cardiac silhouette,
vascular redistribution interstitial edema,
pleural effusions

EKG –normal
tachycardia, atrial and ventricular
enlargement, LBBB, RBBB, Q-waves

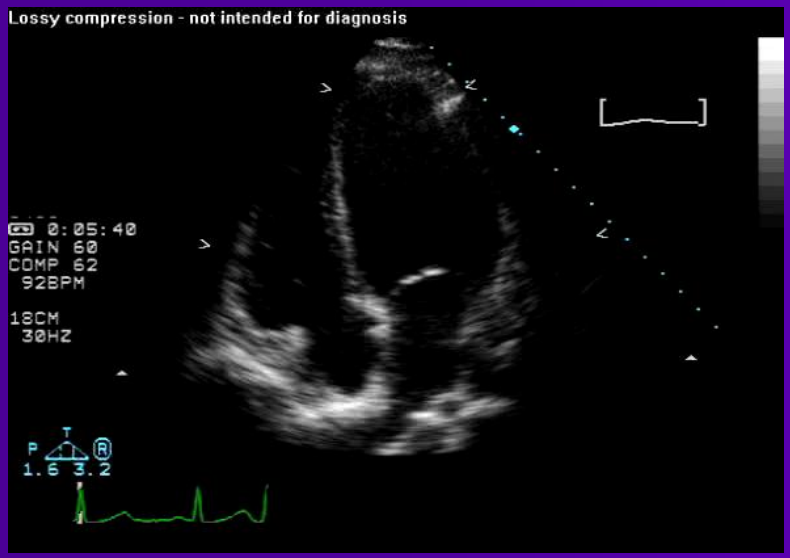
Blood Tests
(ANA,RF, Fe^{2+}, TFT's,ferritin,)

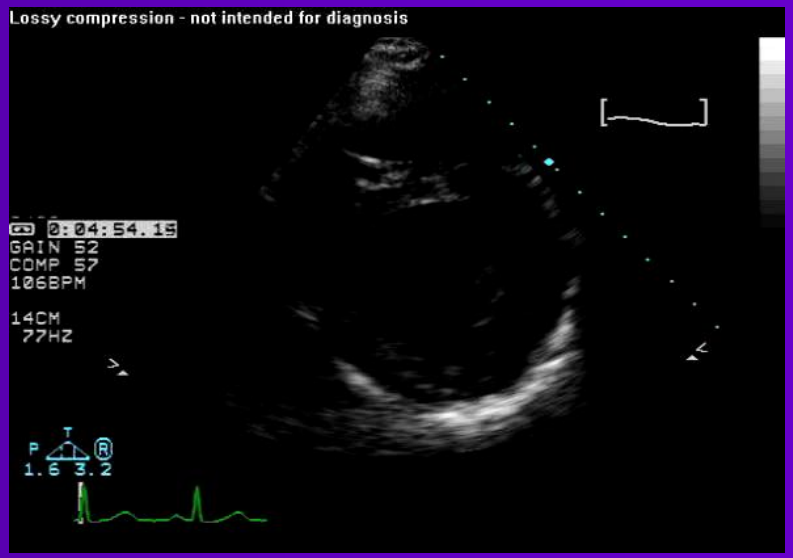
Echocardiography
LV size, wall thickness function
valve dz, pressures

Cardiac Catheterization
hemodynamics
LVEF
angiography

Endomyocardial Biopsy

Echo in dilated CM





Criteria for NYHA Functional Classification

Class 1: No limitation of physical activity.
Ordinary physical activity w/o fatigue, palpitation, or dyspnea.

Class 2: Slight limitation of physical activity. Comfortable at rest, but symptoms w/ ordinary physical activity

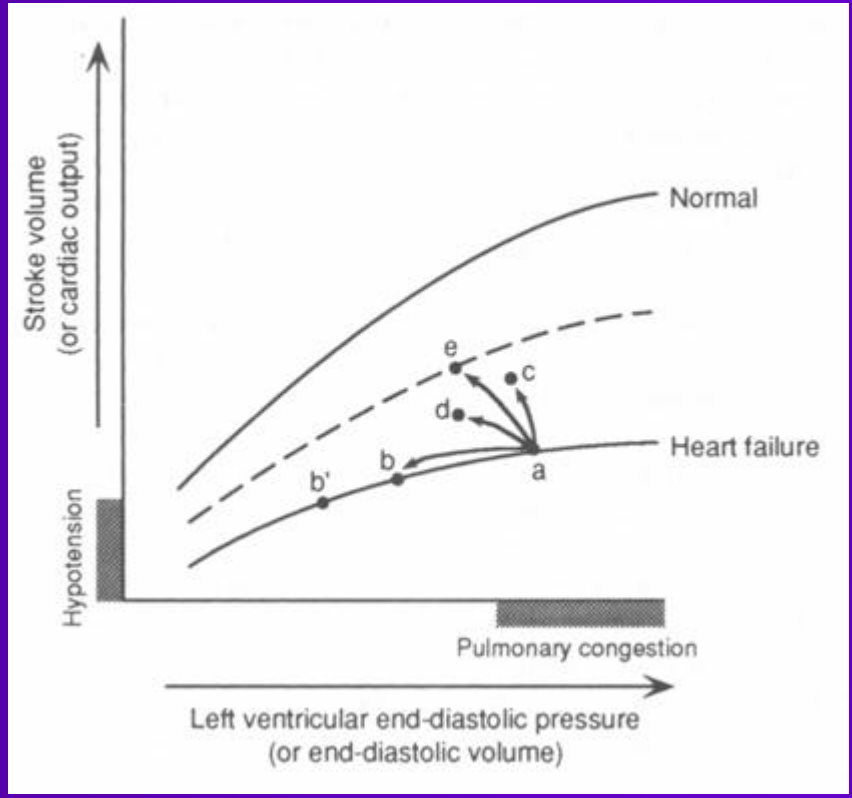
Class 3: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.

Class 4: Unable to carry out any physical activity without discomfort. Symptoms include cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

***J Cardiac Failure* 1999;5:357-382**

Aim of Treatment

- Preload reduction
  - Diuretics
  - venodilators
- Vasodilators
  - ACEI
- Inotropes
  - Acutely
  - Chronically
    - mortality



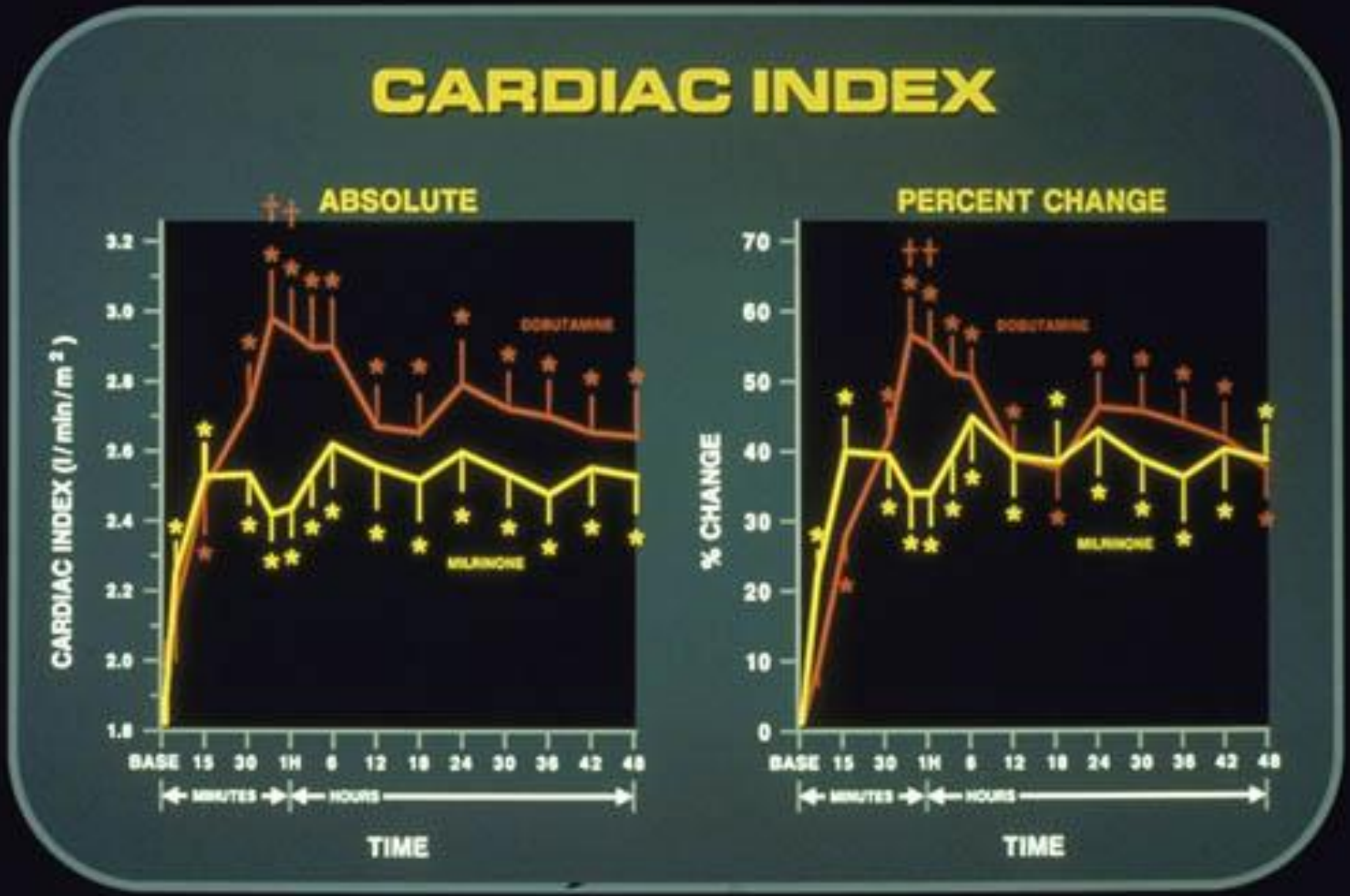
Vasodilator Agents in Heart Failure

Drug	Mechanism	Action	Use
Nitroglycerin and long-acting nitrates*	Direct via nitric oxide	Veno / arterioloar	Hemodynamic; anti-ischemic; long term
Nitroprusside	Direct via nitric oxide	Arteriolar > venodilation	Hemodynamic
Hydralazine*	Direct	Arteriolar	?long term*
ACE inhibitors#	Reduced A-II Incr. bradykinin	Veno / arterioloar	Long-term

*Hydralazine and a long-nitrate shown to reduce mortality long-term

Other actions (aside from vasodilation) likely to be important

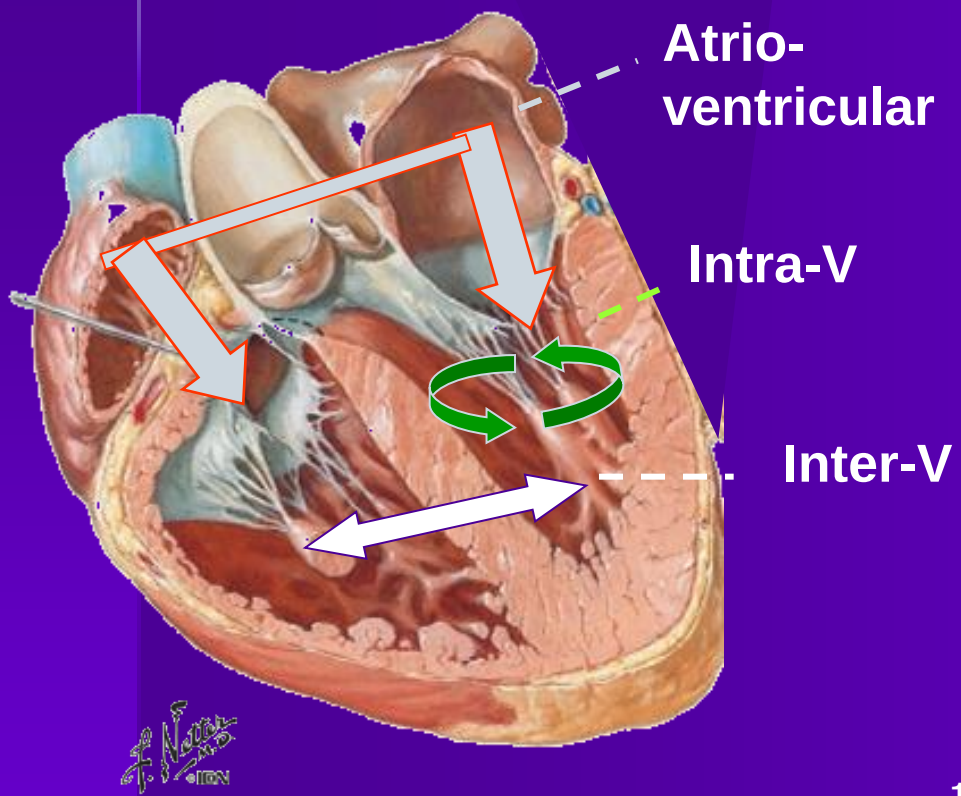
Dobutamine and Milrinone Effects



Electrical and Mechanical Ventricular Dyssynchrony

- Experimentally induced LBBB has effect on:
  - expression of regional stress kinases
  - calcium-handling proteins.
- Expression of p38-MAPK (a stress kinase) is elevated in the endocardium of the late-activated region, whereas phospholamban is decreased.
- Sarcoplasmatic reticulum Ca^{2+}-ATPase is decreased in the region of early activation.

Deleterious Hemodynamic Effects of LV Dyssynchrony



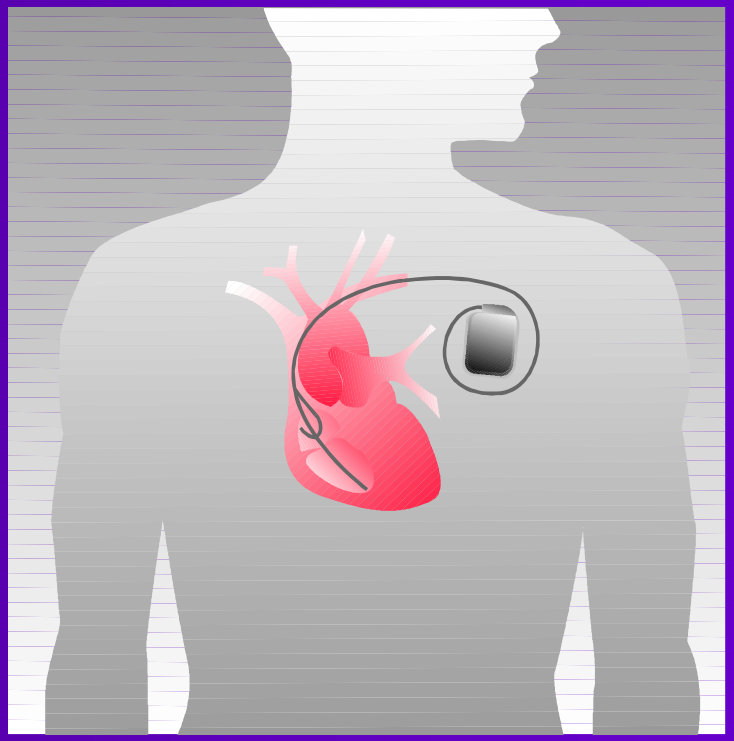
Diminished SV & CO due:

- Reduced diastolic filling time[1]
- Weakened contractility [2]
- Protracted MV regurgitation [2]
- Post systolic regional contraction [3]

1. Grines CL, *Circulation* 1989;79: 845-853
2. Xiao HB, *Br Heart J* 1991;66: 443-447
3. Søgaard P, JACC 2002;40:723–730

CRT: Cardiac Resynchronization Therapy

1. Improved hemodynamics
   - Increased CO
   - Reduced LV filling pressures
   - Reduced sympathetic activity
   - Increased systolic function w/o MVO2
2. Reverse LV remodeling/architecture
   - Decreased LVES/ED volumes
   - Increased LVEF
     - Circ ’02, JACC ’02, JACC ’02, NEJM’02



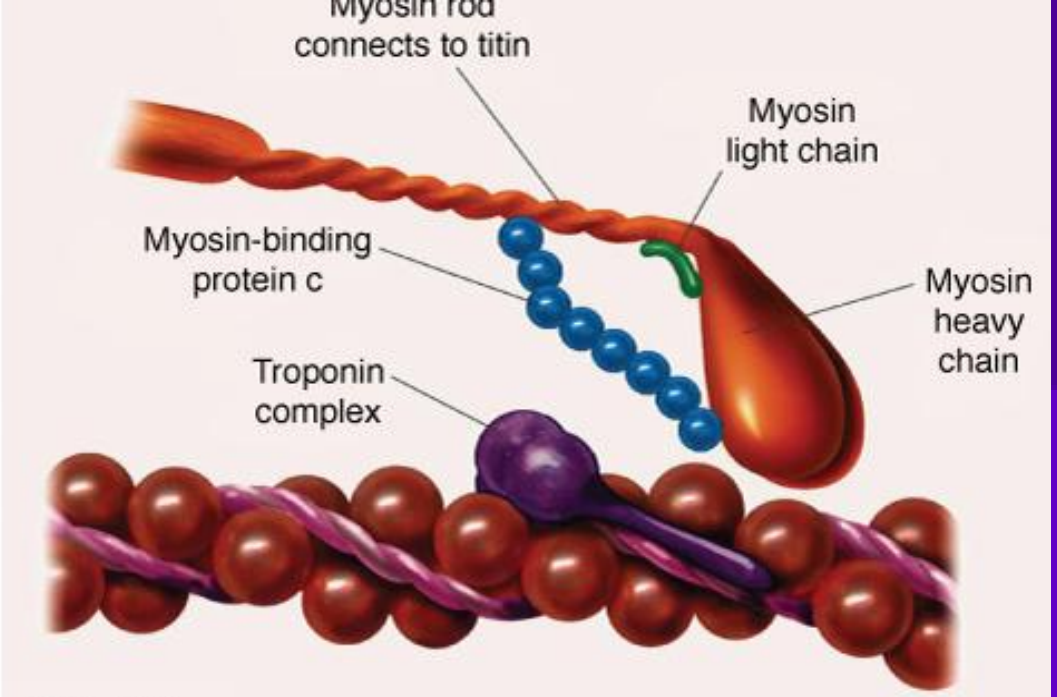
DEFINITION

HCM is a genetic disease state characterized by unexplained LV hypertrophy associated with nondilated ventricular chambers in the absence of another cardiac or systemic disease that itself would be capable of producing the magnitude of hypertrophy evident in given patient.

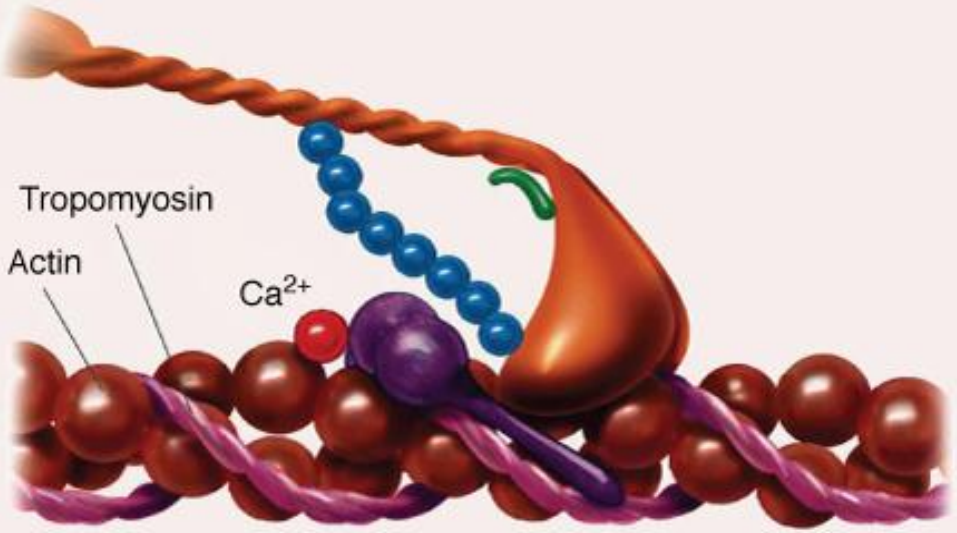
It's prevalance estimated to be 1:500

IHSS, HOCM, and MSS are older terms

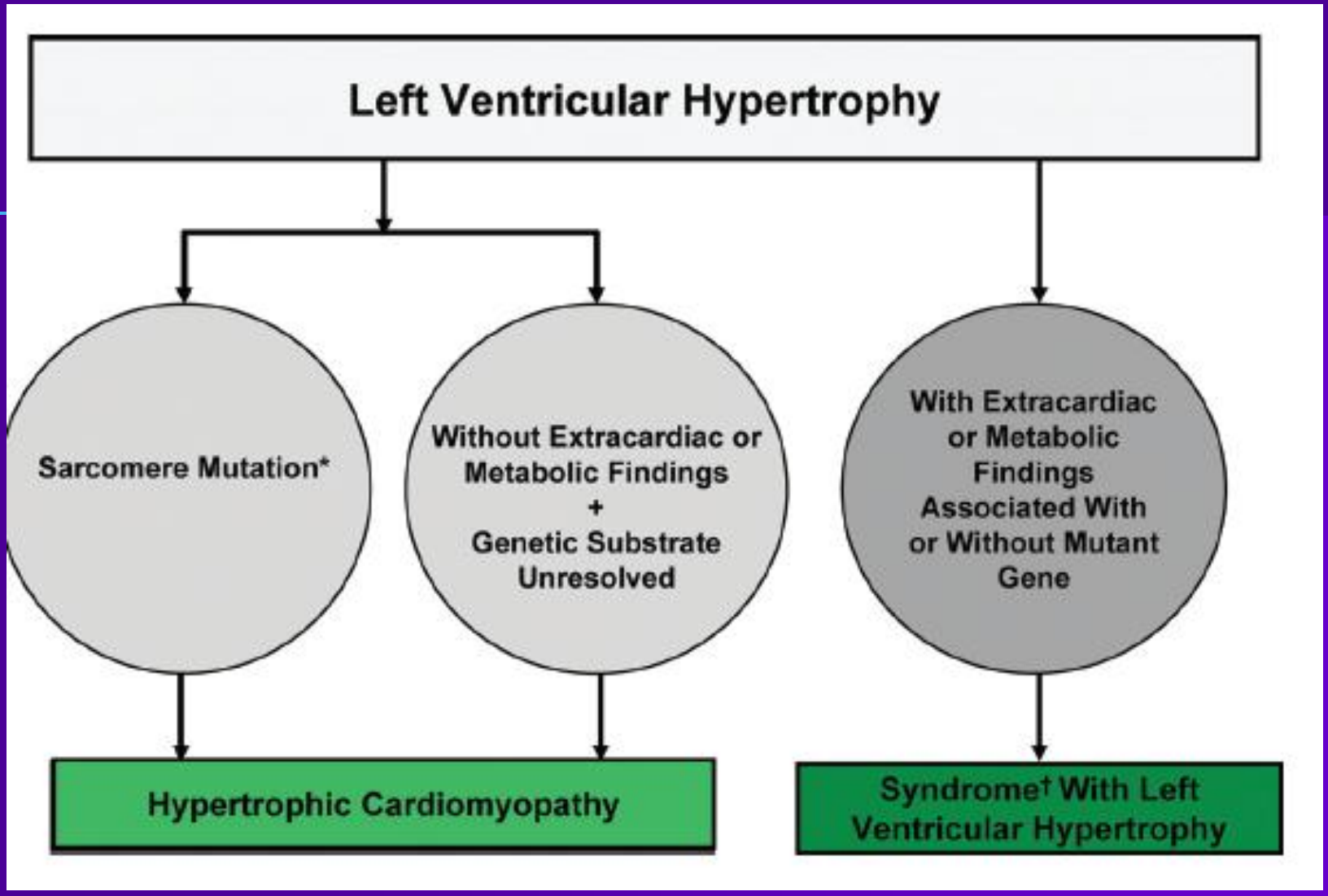
Hypertrophic Cardiomyopathy



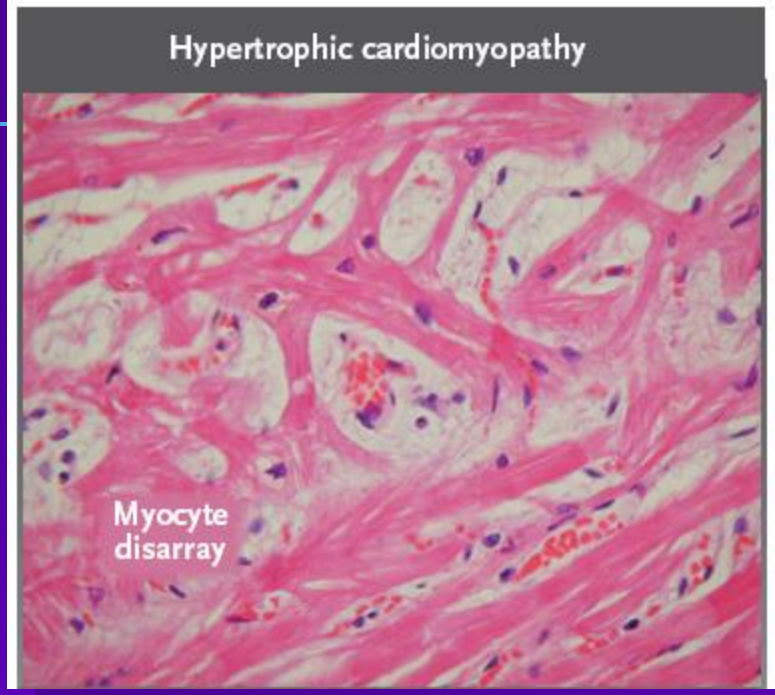
Diastole



Systole


Left Ventricular Hypertrophy
Sarcomere Mutation*
Without Extracardiac or Metabolic Findings + Genetic Substrate Unresolved
With Extracardiac or Metabolic Findings Associated With or Without Mutant Gene
Hypertrophic Cardiomyopathy
Syndrome† With Left Ventricular Hypertrophy

HISTOPATHOLOGY



Whorling and fibrosis

PATHOPHYSIOLOGY

- LV outflow tract obstruction
- Diastolic dysfunction
- Myocardial ischemia
- Mitral regurgitation
- Arrhythmias
- End stage/ burned out

LV OUTFLOW OBSTRUCTION

- Produced by SAM of mitral valve
- Explanations for the SAM of the mitral valve

1. Mitral valve is drawn toward the septum because of the lower pressure that occurs as blood is ejected at high velocity through a narrowed outflow tract (Venturi effect)
2. Mitral valve is pulled against the septum by contraction of the papillary muscles, which occurs because of the valve's abnormal location and septal hypertrophy altering the orientation of the papillary muscles
3. Hydrodynamic “drag” or the “pushing” force of flow

DYNAMIC OBSTRUCTION IS WORSENED BY

- Increase in contractility
  - VPC
  - Dobutamine,Isoproterenol
  - Exercise
- Decrease in afterload/volume
  - Valsalva maneuver
  - Standing
  - Nitroglycerine/amylnitrite inhalation
  - Blood loss

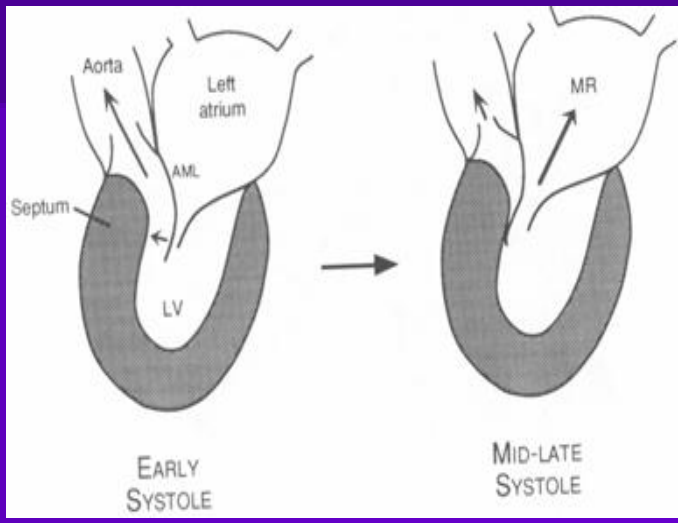
HCM with outflow obstruction

Dynamic LVOT obstruction (may not be present at rest)

SAM (systolic anterior motion of mitral valve)

LVOT Obstruction ⇒ LVOT gradient
⇒ ↑wall stress ⇒ ↑MVO2 ⇒ ischemia/angina

↑ LVOT gradient: ↑ HR (DFP), ↓preload (LVEDV),
↓ afterload(BP).
↓ LVOT gradient: ↑ BP (Afterload), ↑ LVEDV(preload)



Symptoms of dyspnea and angina more related to diastolic dysfunction than to outflow tract obstruction

Syncope: LVOT obstruction (failure to increase CO during exercise or after vasodilatory stress) or arrhythmia.

MYOCARDIAL ISCHEMIA

- Often occurs without atherosclerotic coronary artery disease
- Postulated mechanisms
  - Abnormally small and partially obliterated intramural coronary arteries as a result of hypertrophy
  - Inadequate number of capillaries for the degree of LV mass and increased myocardial oxygen consumption-supply demand mismatch
  - Increased filling pressures resulting in subendocardial ischemia

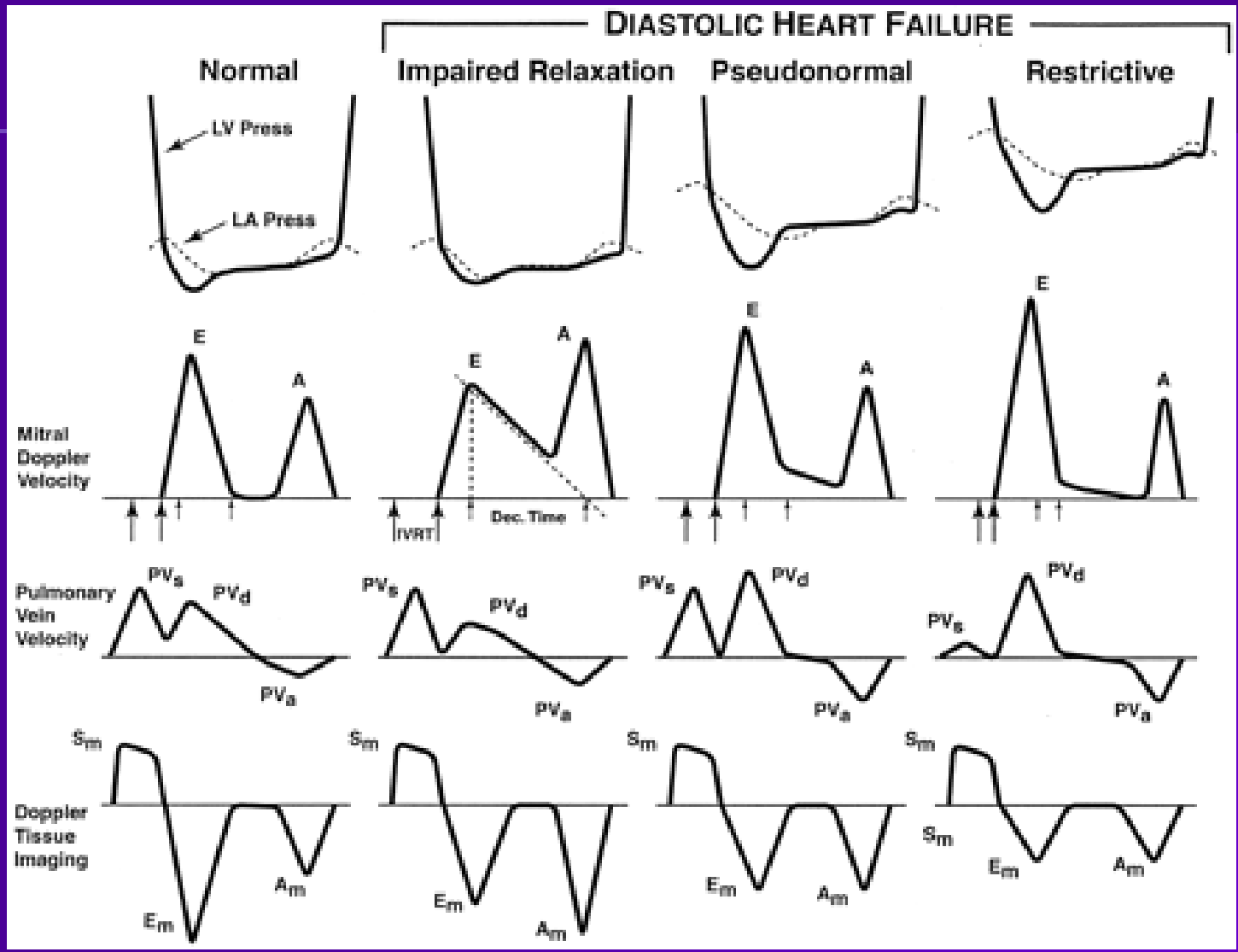
Diastolic Dysfunction

- 40-50% of pts w/ CHF have nml LVEF
  - Vasan JACC '99
  - Grossman Circ '00
- Prevalence:
  - increases with age
  - higher in women
- Etiology: HTN & LVH
- Diagnosis:
  - MV& PV Doppler
  - TDI, Color m-mode

DIASTOLIC DYSFUNCTION

- Impaired relaxation
- Decreased compliance
  - Hypertrophy
  - Disorganised cellular architecture
  - Replacement scarring
  - Interstitial fibrosis
- Accounts for symptoms of exertional dyspnea
  - Increased filling pressures → increased pulmonary venous pressure

Echo Doppler Parameters

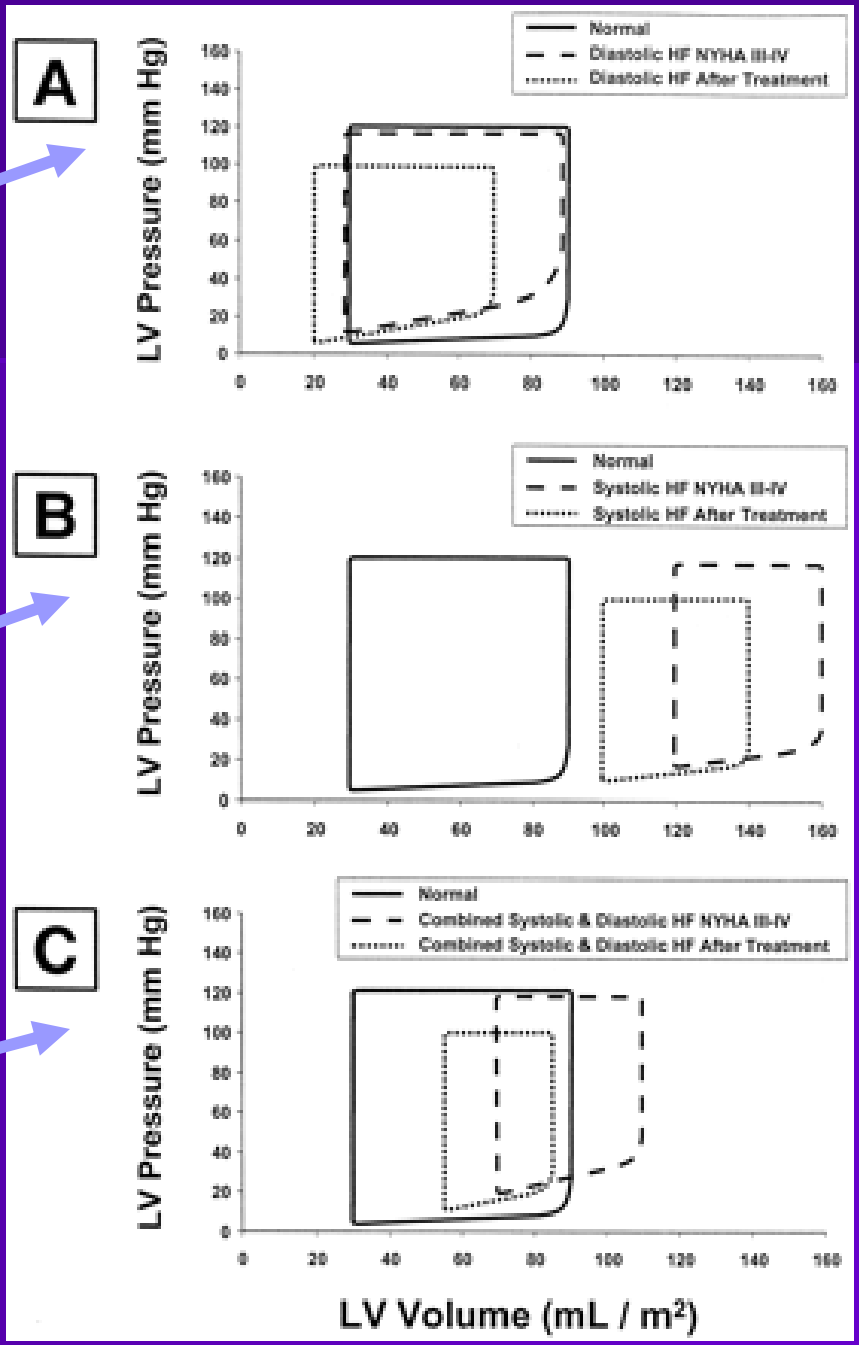


Zile MR. Circ;105:1387

Isolated Diastolic HF

Isolated Systolic HF

Systolic & Diastolic HF



Zile MR. Circ;105:1387

MITRAL VALVE APPARATUS

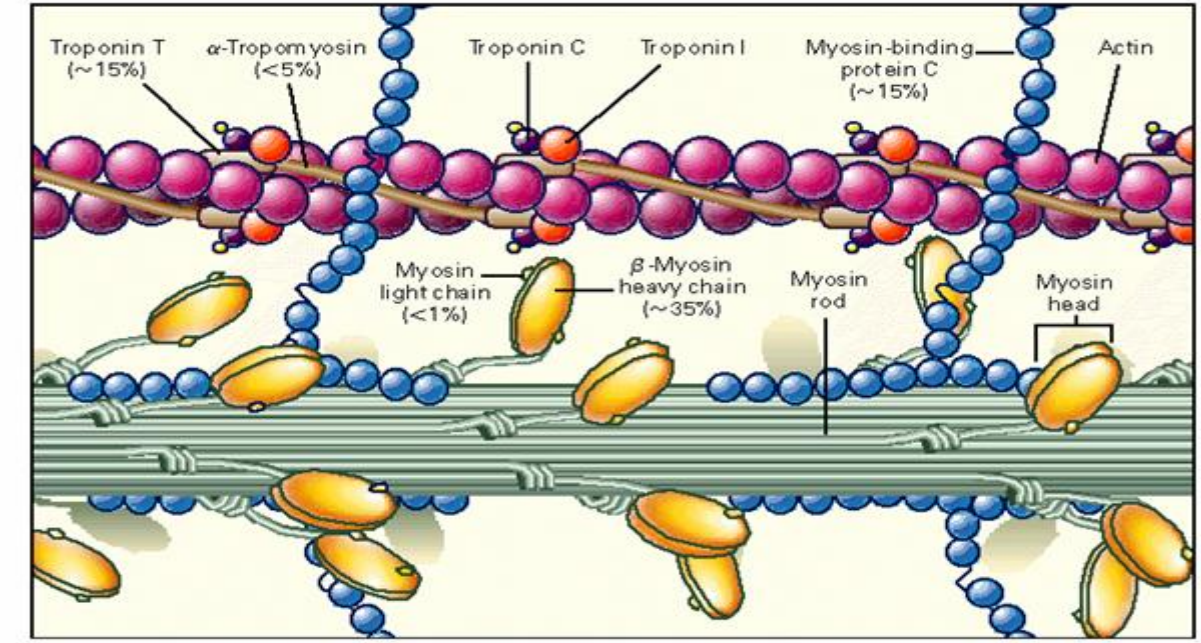
- Twice the normal size due to elongation of both leaflets or segmental enlargement of only anterior leaflet or mid portion of posteror leaflet
- Congenital and anomalous anterolateral papillary muscle insertion into the anterior leaflet without interposition of chordae tendineae and produce muscular midcavity outflow obstruction >>SAM>>LVOTO
- Variations in leaflet length (posterior/anterior leaflet length mismatch) – restrict the ability of the posterior leaflet to follow the anterior leaflet and to coapt effectively resulting in MR
- Severity of MR directly proportional to LV outflow obstruction
- Results in symptoms of dyspnea, orthopnea

Etiology

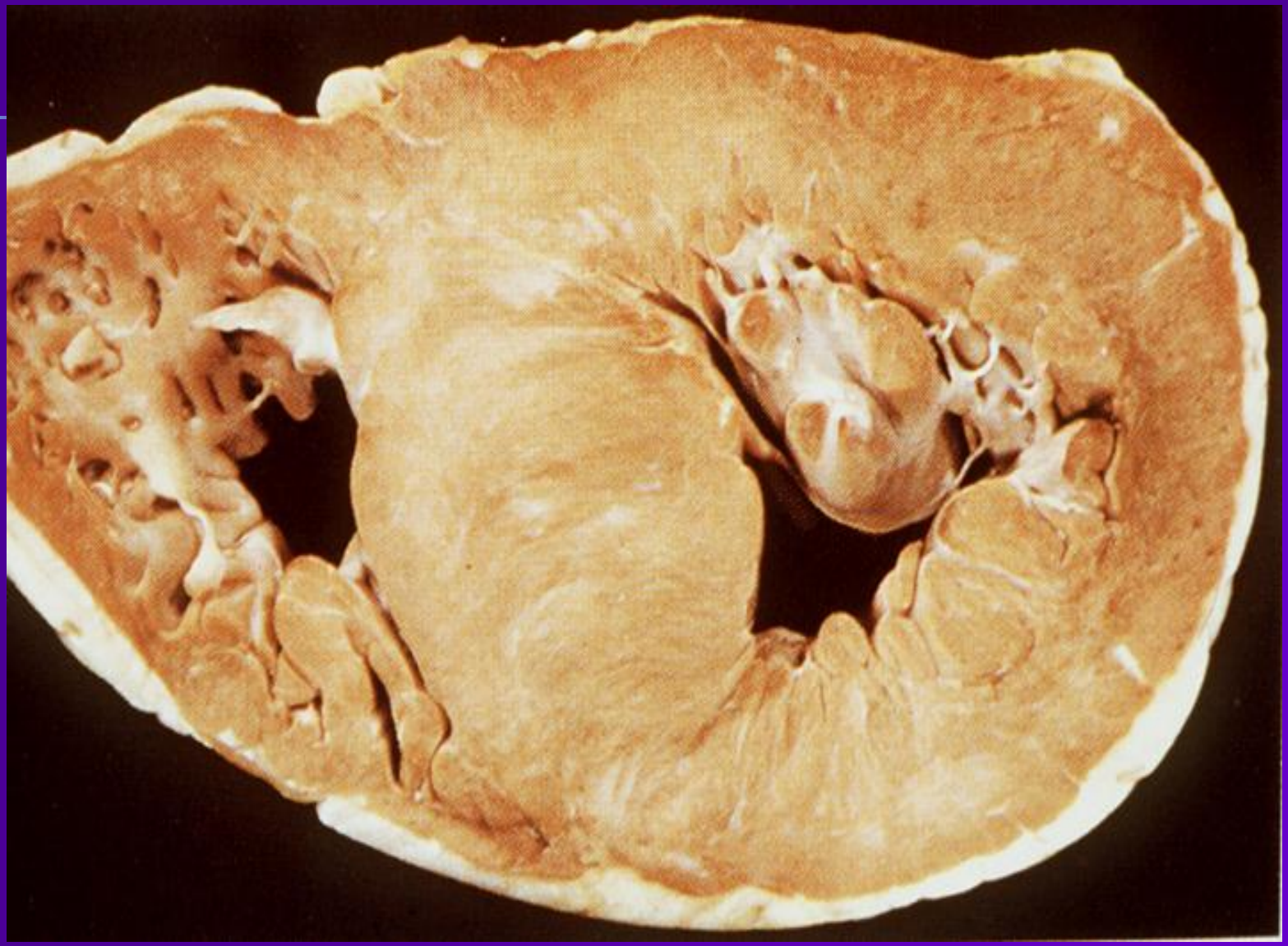
Familial in ~ 55% of cases with autosomal dominant transmission
Mutations in one of 4 genes encoding proteins of cardiac sarcomere
account for majority of familial cases

β-MHC
cardiac troponin T
myosin binding protein C
α-tropomyosin

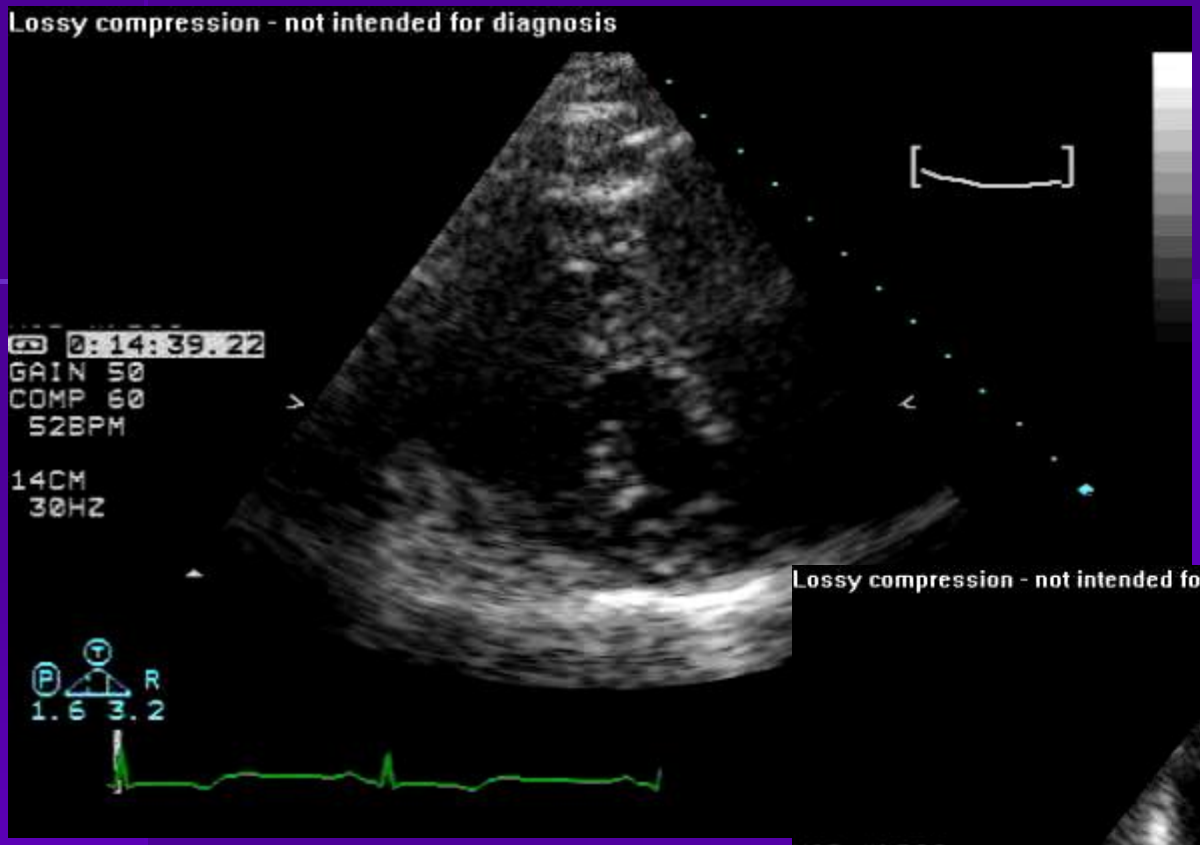
Remainder are spontaneous mutations.

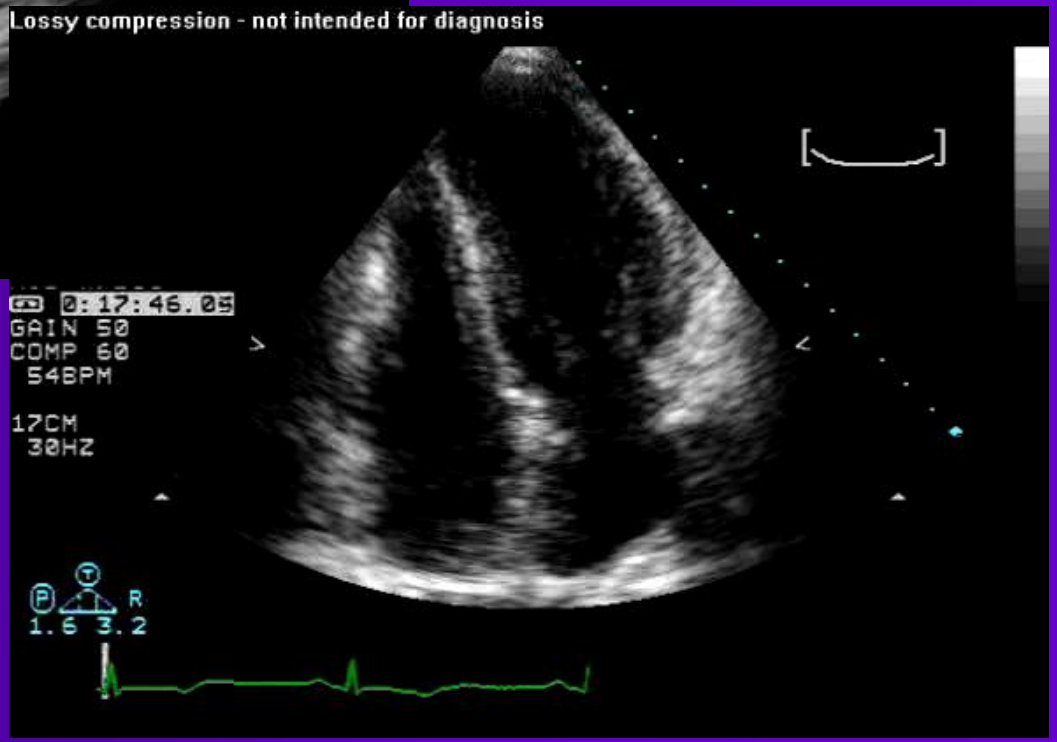


Hypertrophic Cardiomyopathy



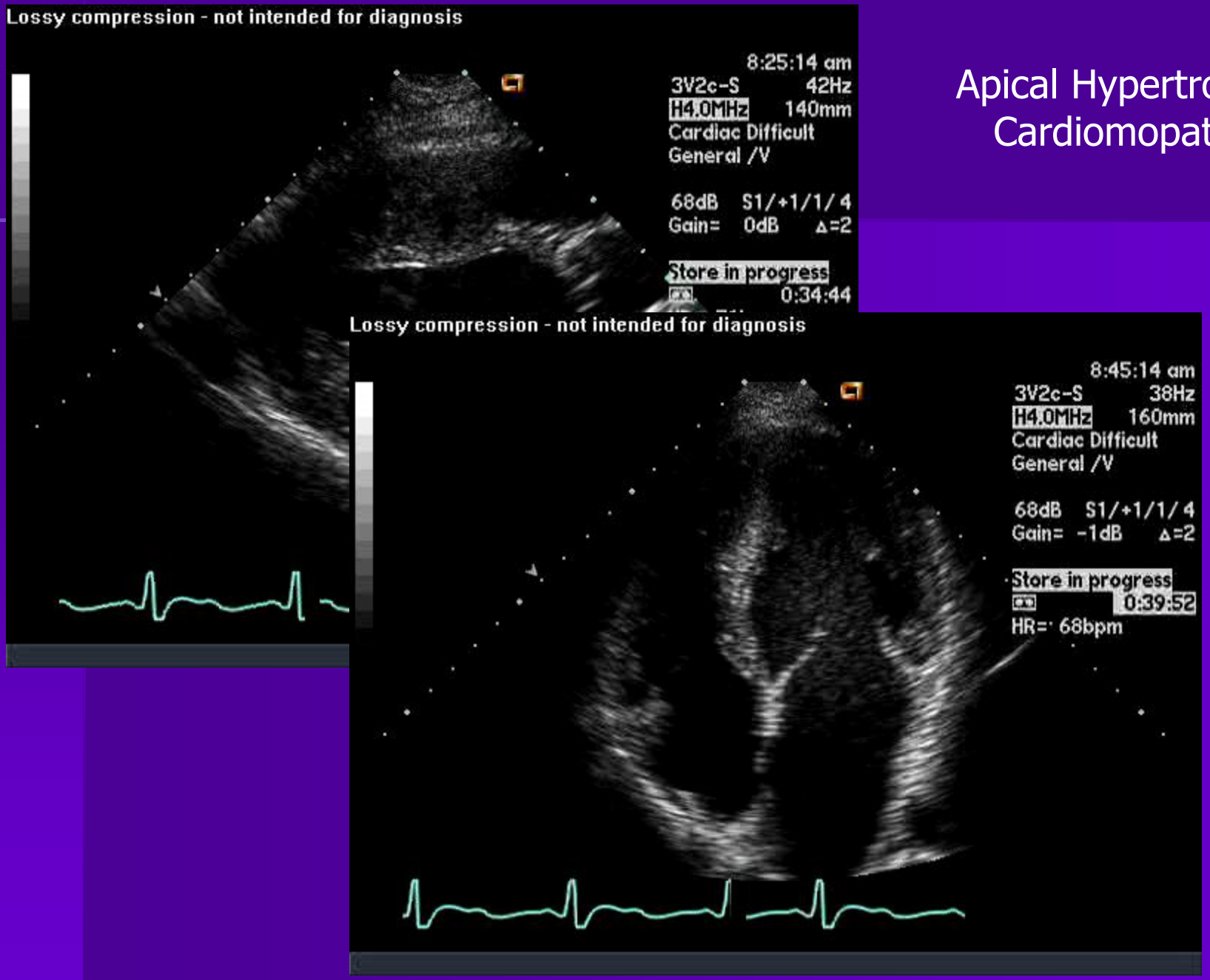
Hypertrophic Cardiomyopathy



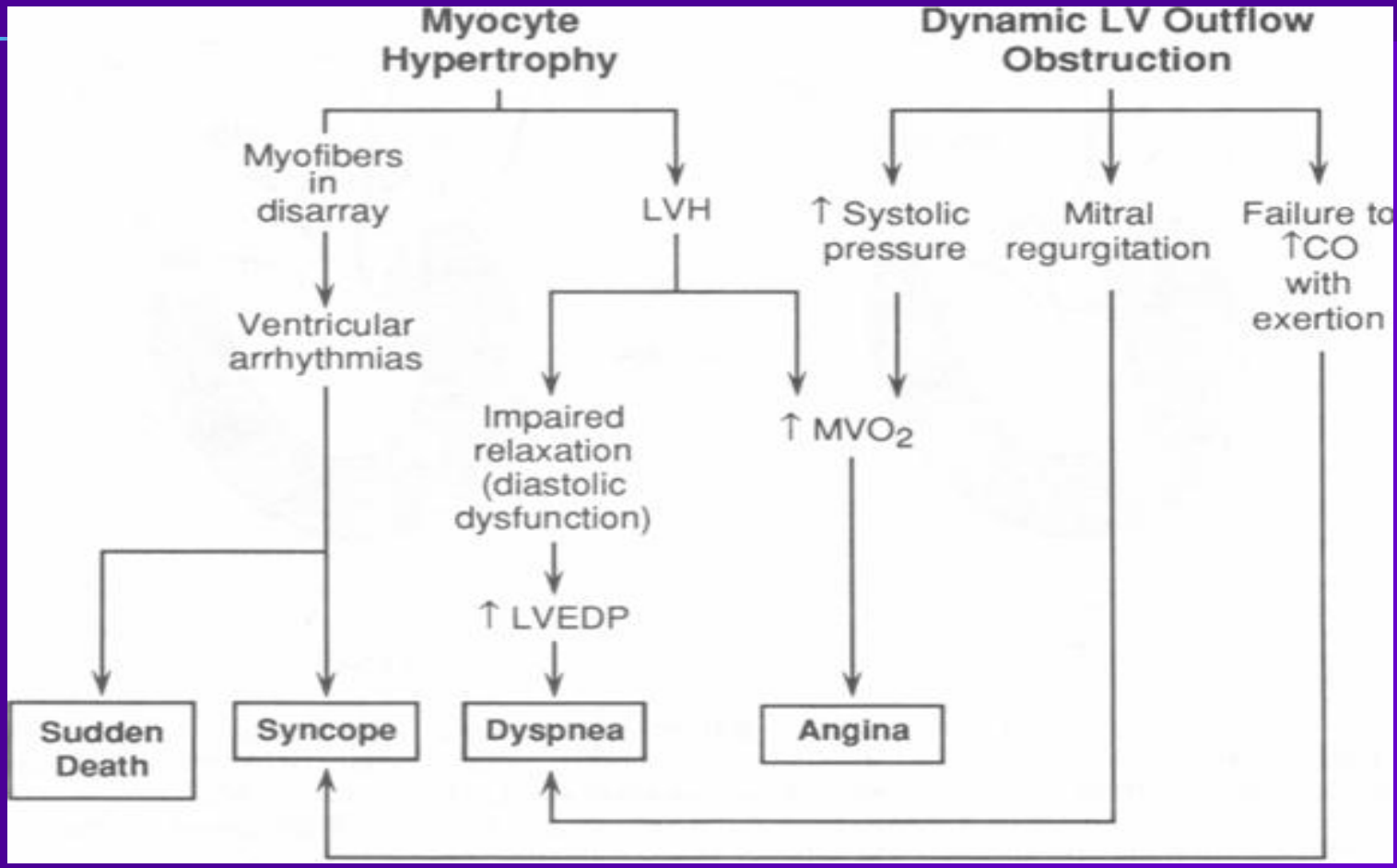


Hypertrophic cardiomyopathy

Apical Hypertrophic Cardiomopathy



Pathophysiology



Physical Exam

Bisferiens pulse ("spike and dome")
S4 gallop
Crescendo/Descrescendo systolic ejection murmur

HOCM vs. Valvular AS

	Intensity of murmur	
	HOCM	AS
Valsalva (↓preload, ↓ afterload)	↑	↓
Squatting (↑ preload, ↑ afterload)	↓	↑
Standing (↓preload, ↓ afterload)	↑	↓

Holosystolic apical blowing murmur of mitral regurgitation

PHYSICAL

- Jugular venous pulse: prominent a- wave
- Double carotid arterial pulse: declines in mid systole as gradient develop
- Double apical impulse:
  - Forceful left atrial contraction against non-compliant ventricle
- Triple apical impulse:
  - Late systolic bulge near isometric contraction
- S1: normal
- S2: normal or paradoxical split
- S3 gallop: decompensated Lt. ventricle
- S4: atrial systole against hypertrophic ventricle

MIMICKING HYPERTROPHIC CARDIOMYOPATHY

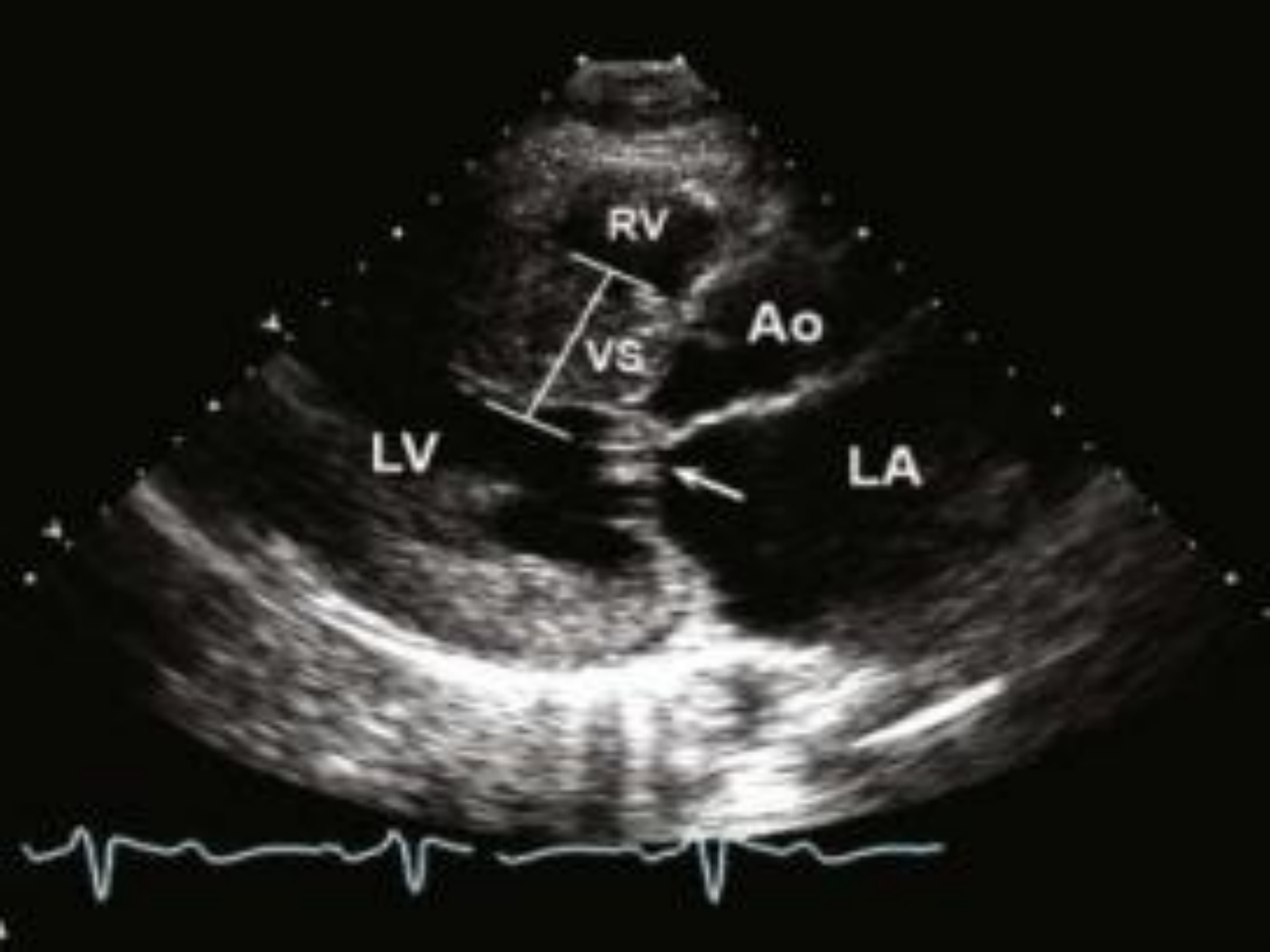
- Chronic hypertension
- RV hypertrophy
- Cardiac amyloidosis
- Athlete's heart
- Valvular AS

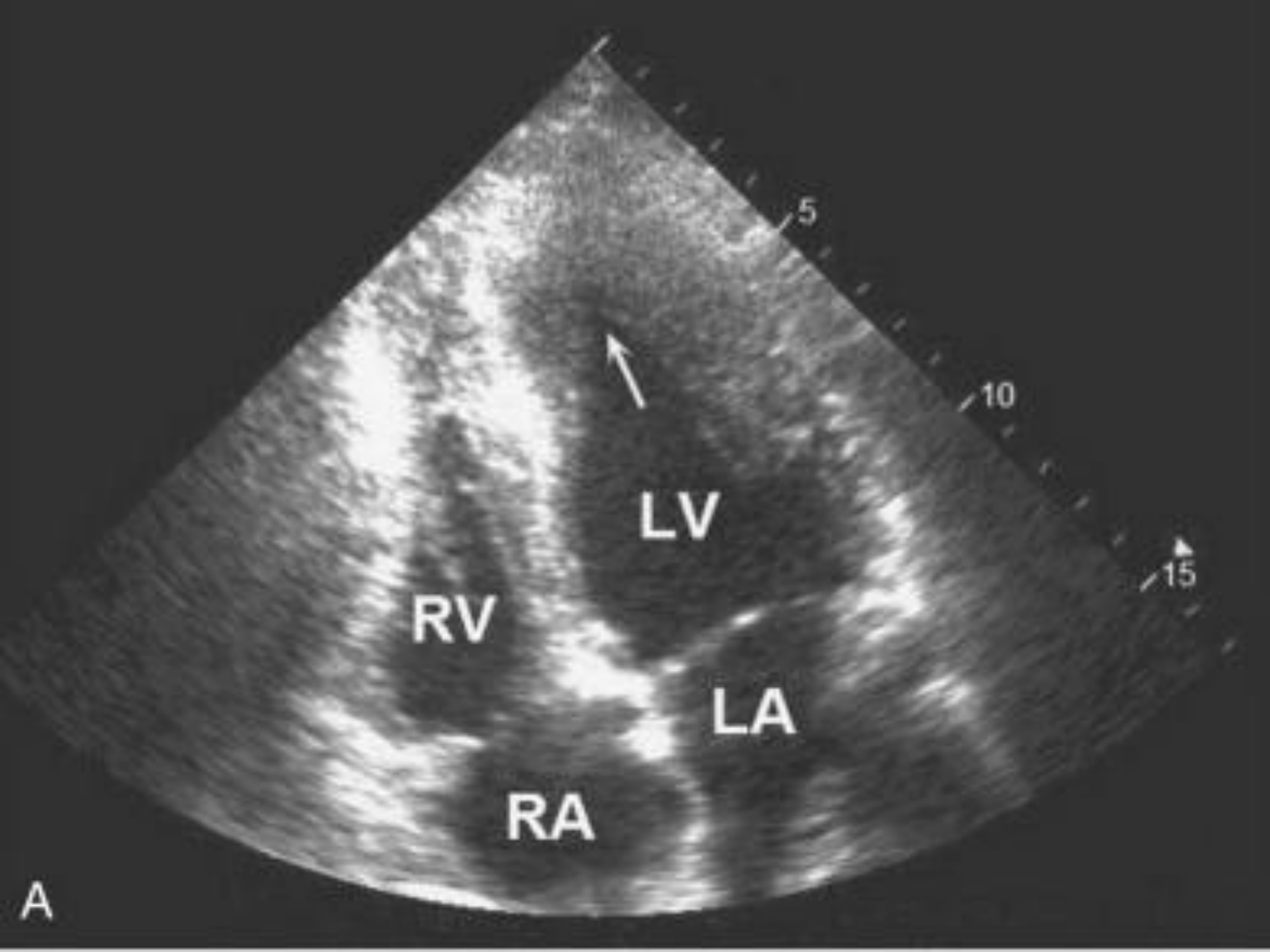
Apical hypertrophy - apical cavity obliteration caused by hypereosinophilic syndrome or noncompaction.

POINTS FAVOURING HCM IN HTN

- Family history of HCM
- Asymmetry
- Right ventricular hypertrophy
- Late gadolinium enhancement at the RV insertion points or localized to segments of maximum LV thickening on CMR
- Maximum LV wall thickness ≥15 mm (Caucasian); ≥20 mm (black)
- Severe diastolic dysfunction
- Marked repolarisation abnormalities, conduction disease or Q-waves on 12 lead ECG
- Regression of LVH

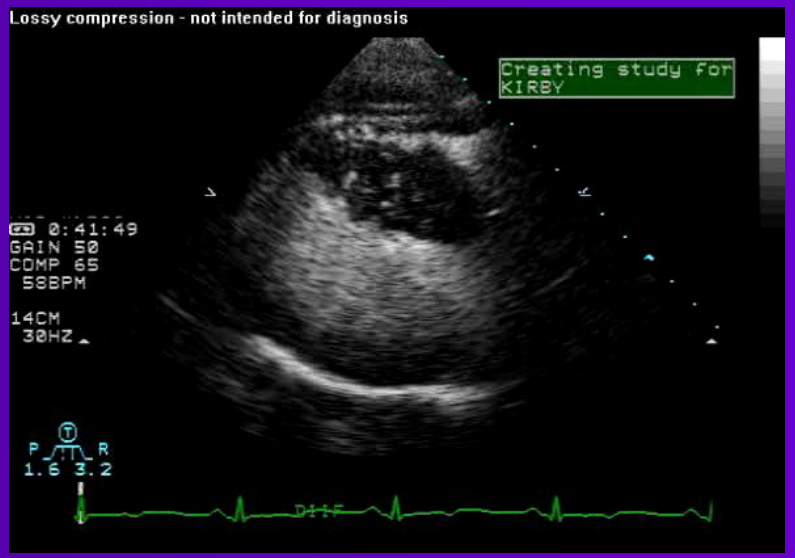
- ESC Guidelines2014


RV
VS
Ao
LV
LA


5
10
15
LV
RV
LA
RA
A

Diagnostic Studies

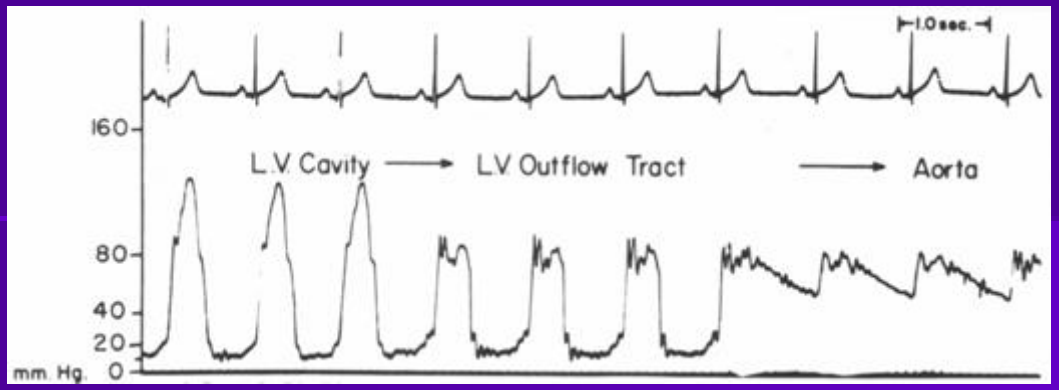
- EKG
  - NSR
  - LVH
  - septal Q waves
- 2D-Echocardiography
  - LVH; septum >1.4x free wall
  - LVOT gradient by Doppler
  - Systolic anterior motion of the mitral valeregurgitation
- Cardiac Catheterization
  - LVOT gradient and pullback
  - provocative maneuvers
  - Brockenbrough phen



HCM-ASH using contrast

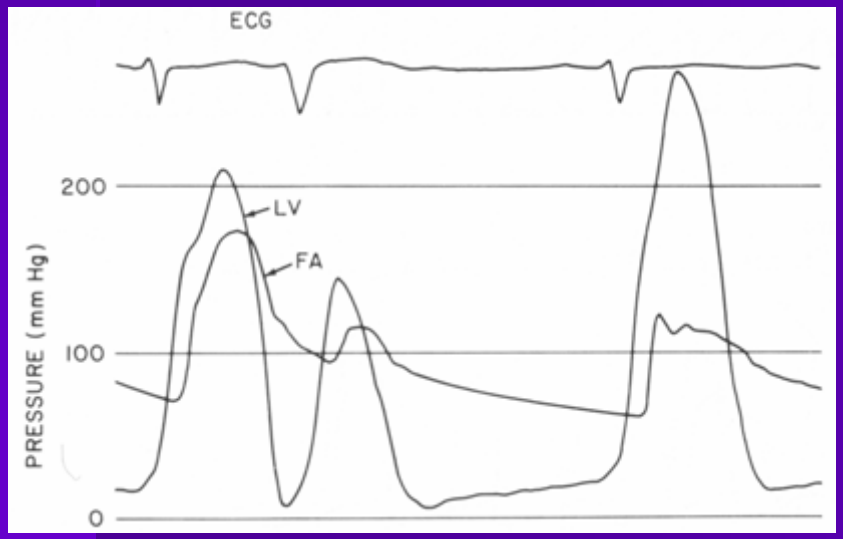
Cardiac Catheterization

LV pullback



Brockenbrough-Braunwald Sign

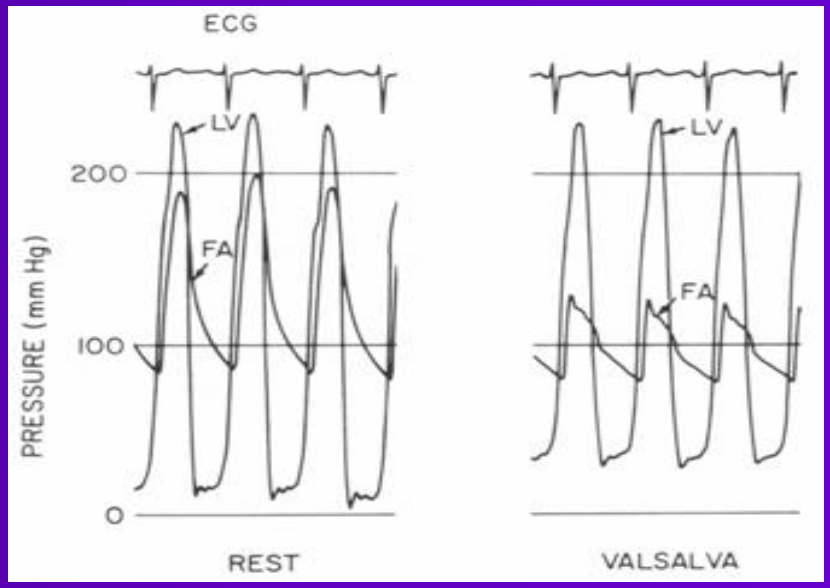
failure of aortic pulse pressure to rise post PVC



Provocative maneuvers:

Valsalva

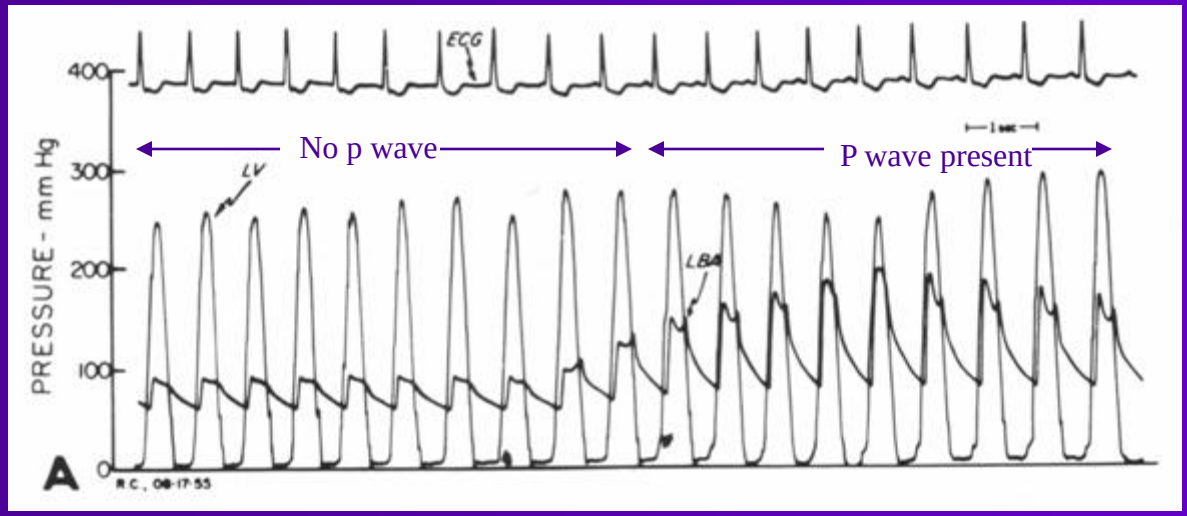
amyl nitrate inhalation



Atrial Fibrillation

Acute A. Fib is poorly tolerated -Acute Pulmonary Edema and Shock
Chronic a fib - Fatigue, dyspnea and angina

Rapid HR - decreased time for diastolic filling and LV relaxation
Loss of atrial "Kick" – decreased LV filling
- decreased SV and increased outflow tract obstruction



Rate slowing with β-blockers and Ca2+ channel blockers
Digitalis is relatively contra-indicated- positive inotrope
DC Cardioversion

Treatment

For symptomatic benefit

β-blockers

↓ mvO2

↓ gradient (exercise)

arrythmias

Calcium Channel blockers

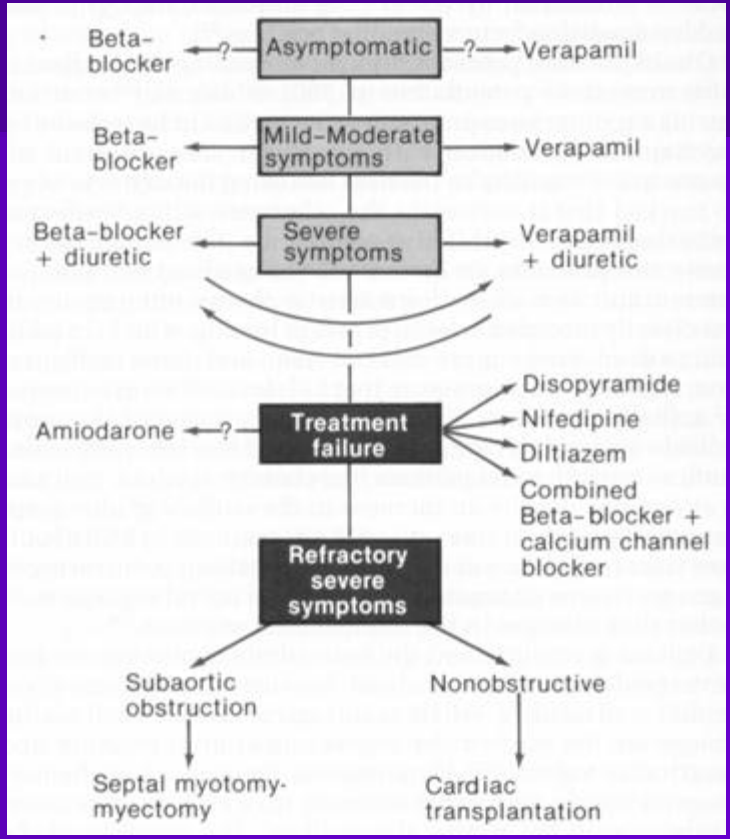
Anti-arrhythmics

afib

amiodorone

Disopyramide

AICD for sudden death



antibiotic prophylaxis for endocarditis

No therapy has been shown to improve mortality

HCM: Surgical Treatment

For severe symptoms with large outflow gradient (>50mmHg)
Does not prevent Sudden Cardiac Death

Myomyectomy
- removal of small portion of upper IV septum
- +/- mitral valve replacement
- 5 year symptomatic benefit in ~ 70% of patients

Dual Camber (DDD pacemaker) pacing
- decreases LVOT gradient (by~25%)
- randomized trials have shown little longterm benefit
- possible favorable morphologic changes

ETOH septal ablation

AICD to prevent sudden death

Hypertrophic CM

- Most common cause of death in young people.
- The magnitude of left ventricular hypertrophy is directly correlated to the risk of SCD.
- Young pts with extreme hypertrophy and few or no symptoms are at substantial long-term risk of SCD.

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Spirito P. *N Engl J Med.* 1997;336:775-785.
Maron BJ. *N Engl J Med*. 2000;342:365-373.

Prognosis

Sudden Death 2-4%/year in adults
4-6% in children/adolescents

AICD for: survivors of SCD with Vfib
episodes of Sustained VT
pts with family hx of SCD in young family members
High risk mutation (TnT, Arg403Gln)

Predictors of adverse prognosis:

- early age of diagnosis
- familial form with SCD in 1st degree relative
- history of syncope
- ischemia
- presence of ventricular arrhythmias on Holter (EPS)

EPS

Amiodorone (low dose)

Prophylactic AICD?

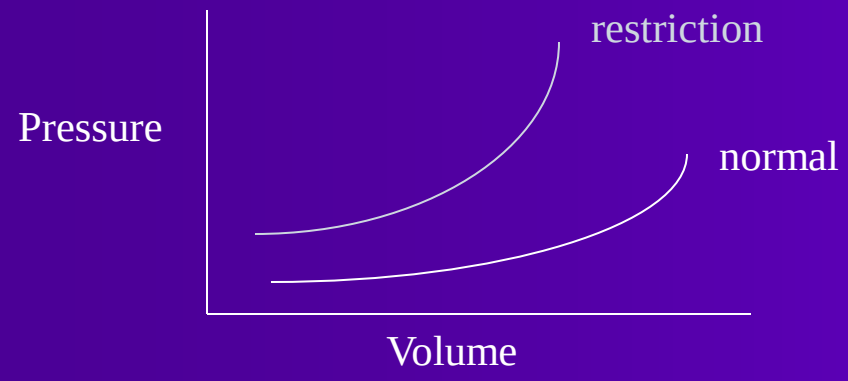
HCM vs Athletes Heart

- Endurance training:
  - Physiologic increase in LV mass
    - Wall thickness and cavity size
- Early HCM vs Athlete's heart
  - DEFINITION: Symmetric, <13mm
  - 947 elite athletes: 16 thickness=13-16mm
    - 15 rowers, EDD=55-63 c/w 728 athletes/22 other
      - NEJM1991;324:295
  - 286 cyclists: 25 thickness 13-15
    - 50% increased EDD w/ 12% reduced LVEF
      - JACC 2004;44:144.

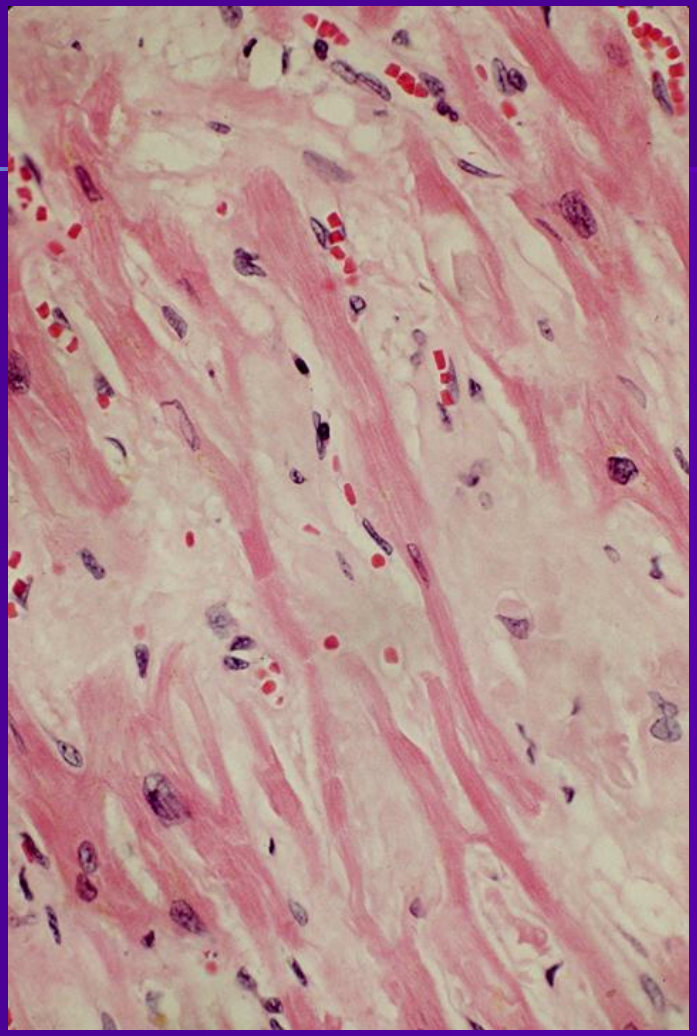
Restrictive Cardiomyopathy

Characterized by:

- impaired ventricular filling due to an abnormally stiff (rigid) ventricle
- normal systolic function (early on in disease)
- intraventricular pressure rises precipitously with small increases in volume



Causes : infiltration of myocardium by abnormal substance
fibrosis or scarring of endocardium



Amyloid infiltrative CM

TABLE 4. CAUSES OF RESTRICTIVE CARDIOMYOPATHY.

Myocardial

Noninfiltrative disorders
- Idiopathic disease
- Familial disease
- Hypertrophy
- Scleroderma
- Diabetes mellitus
- Pseudoxanthoma elasticum

Infiltrative disorders
- Amyloidosis
- Sarcoidosis
- Gaucher's disease
- Hurler's syndrome
- Fatty infiltration

Storage disorders
- Hemochromatosis
- Fabry's disease
- Glycogen storage disease

Endomyocardial

Endomyocardial fibrosis
Hypereosinophilic (Löffler's) syndrome
Carcinoid syndrome
Metastatic cancer
Exposure to radiation
Toxins
Anthracycline (doxorubicin or daunorubicin)
Serotonin
Methysergide
Ergotamine
Mercurial agents
Busulfan

Amyloidosis

Primary Amyloidosis

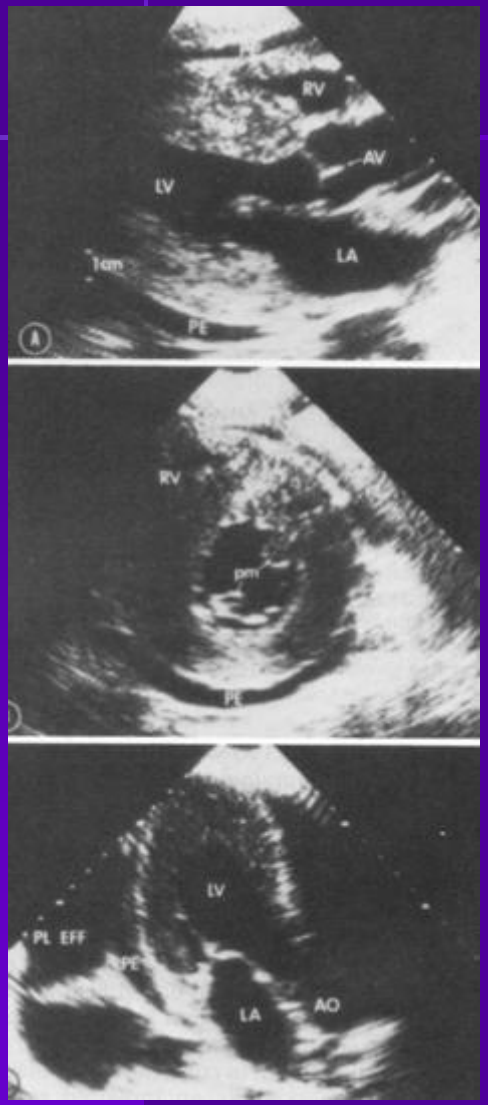
- immunoglobulin light chains -- multiple myeloma

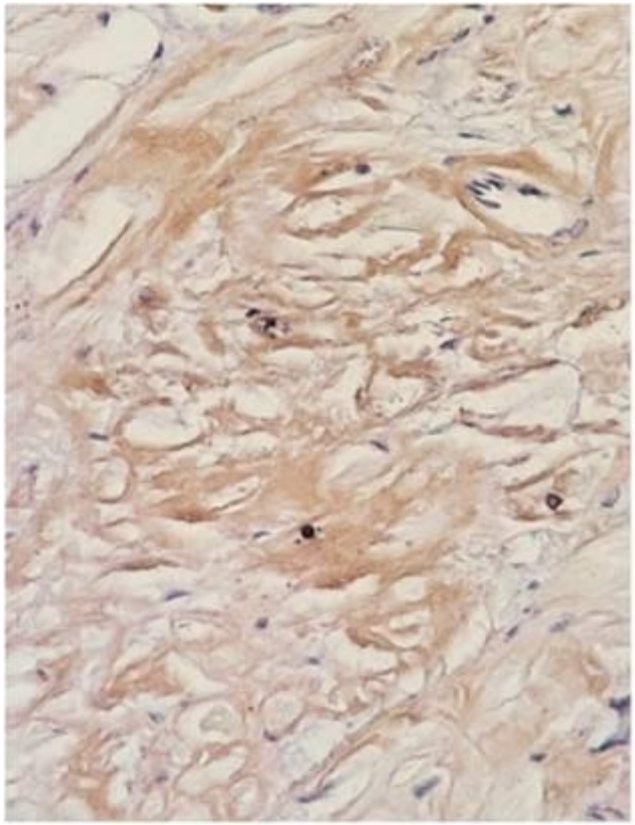
Secondary Amyloidosis

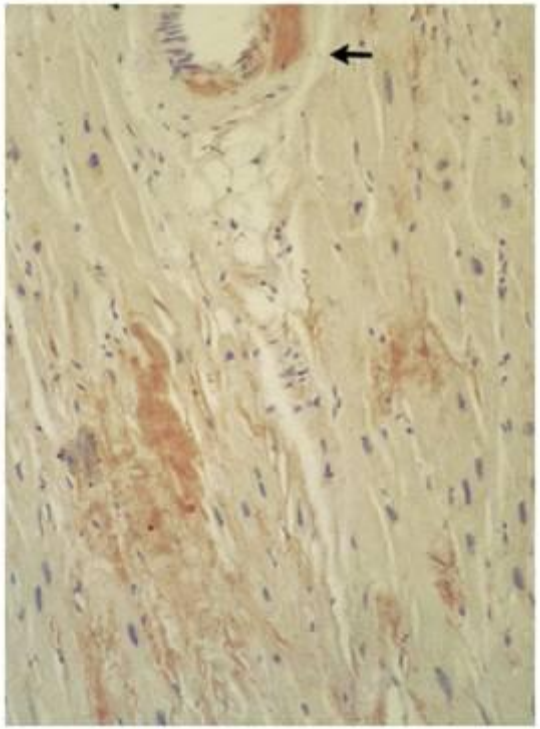
- deposition of protein other than immunoglobulin
  - senile
  - familial
  - chronic inflammatory process

restriction caused by replacement of normal myocardial contractile elements by infiltrative interstitial deposits

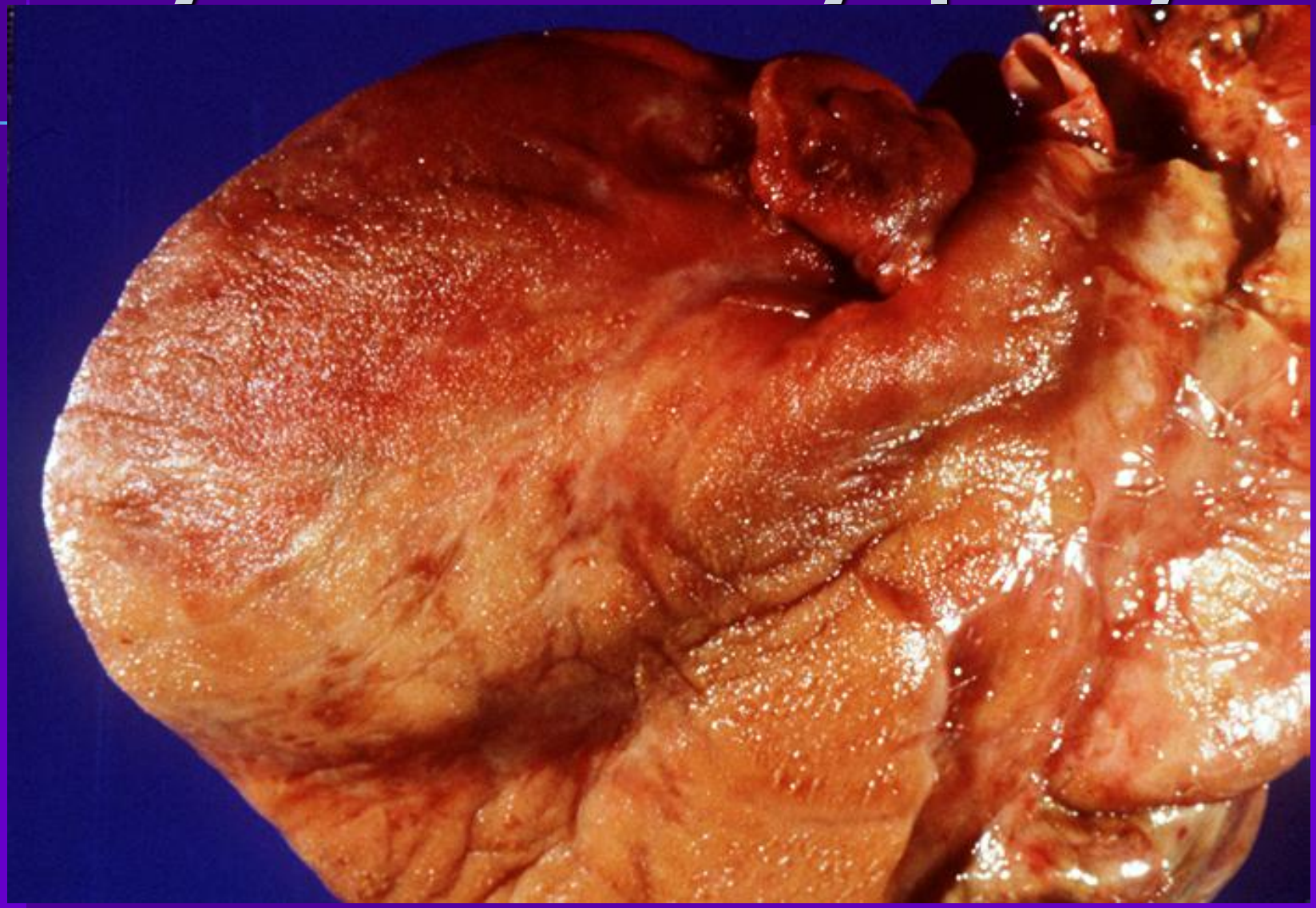
Amyloidosis



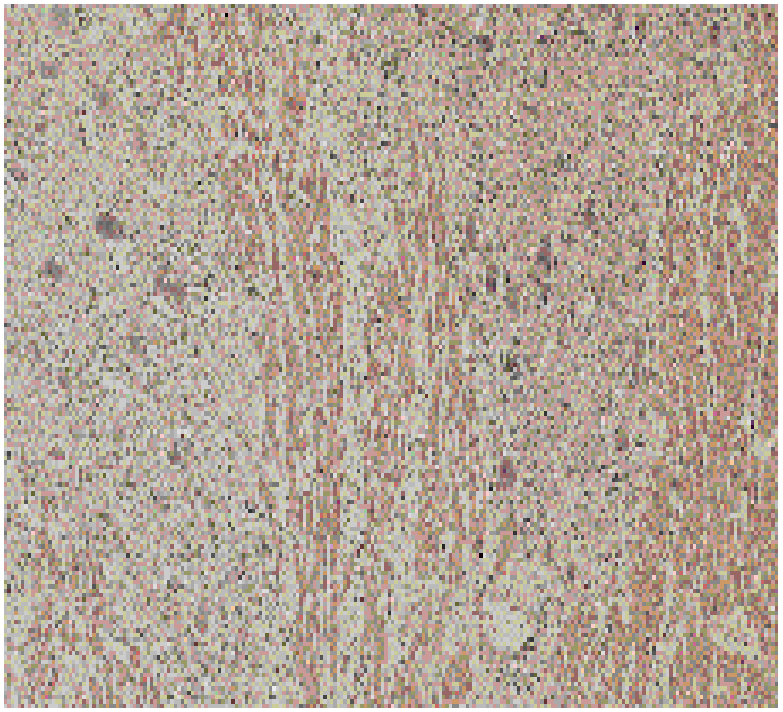




Amyloid Cardiomyopathy



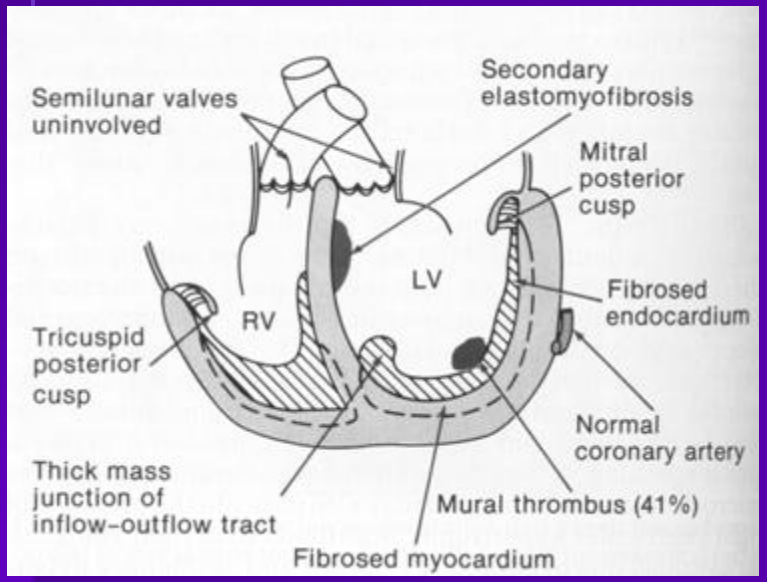
Sarcoidosis



Restriction
Conduction System Disease
Ventricular Arrhythmias
(Sudden Cardiac Death)

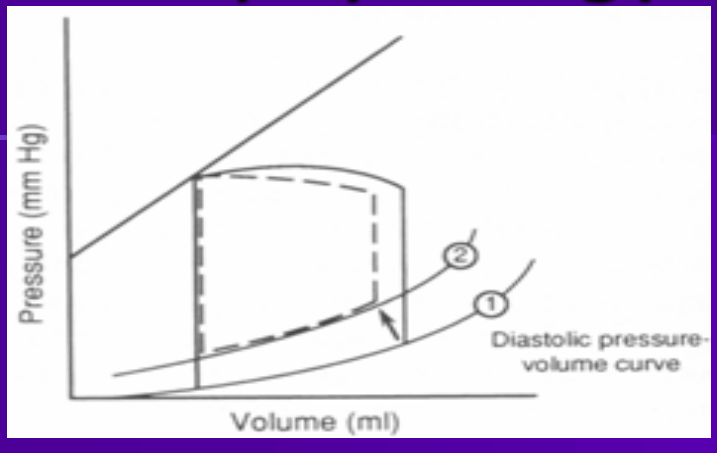
Endomyocardial Fibrosis

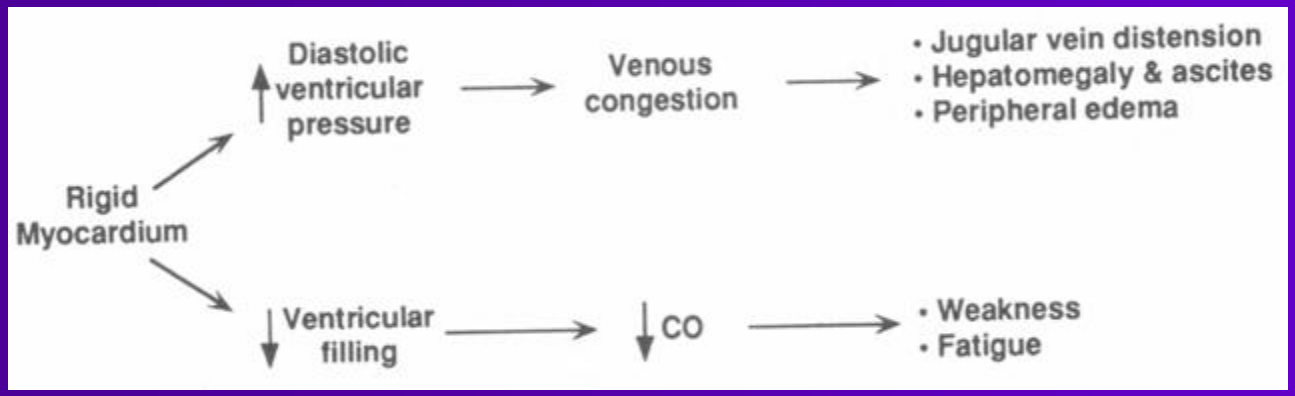
Endemic in parts of Africa, India, South and Central America, Asia
15-25% of cardiac deaths in equatorial Africa
hypereosinophilic syndrome (Loffler's endocarditis)



Thickening of basal inferior wall
endocardial deposition of thrombus
apical obliteration
mitral regurgitation
80-90% die within 1-2 years

Pathophysiology of Restriction





Elevated systemic and pulmonary venous pressures
right and left sided congestion
reduced ventricular cavity size with ↓SV and ↓CO

Clinical Findings

Right > Left heart failure

- Dyspnea
- Orthopnea/PND
- Peripheral edema
- Ascites/Hepatomegaly

Fatigue/ ↓exercise tolerance

Clinically mimics constrictive Pericarditis

Diagnostic Studies

2D-Echo/Doppler-

mitral in-flow velocity

rapid early diastolic filling

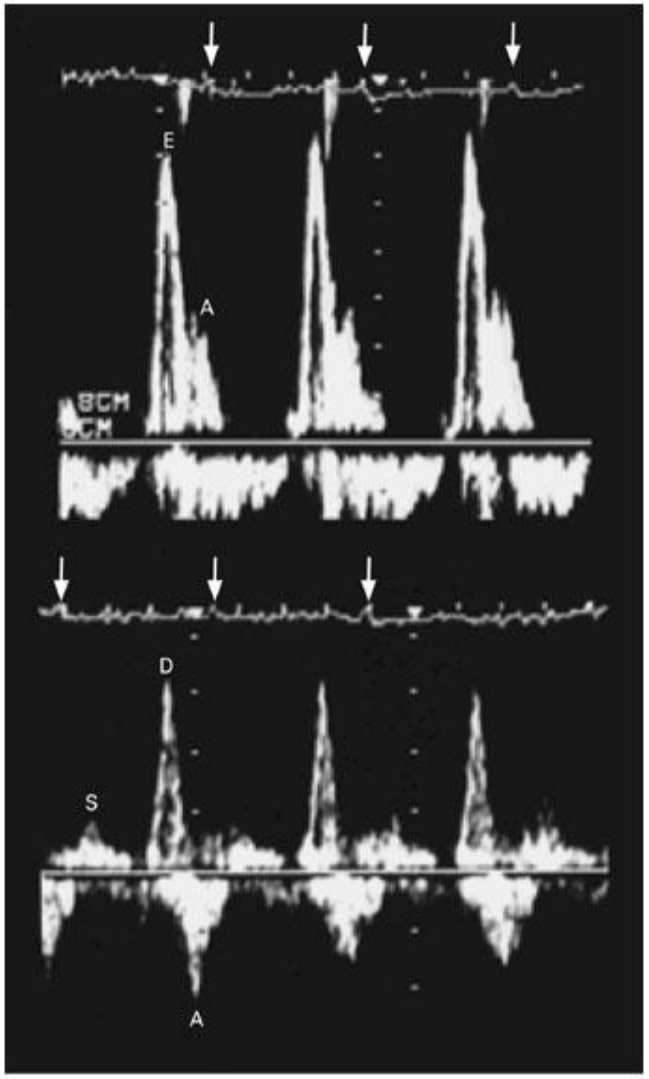
Catheterization –

diastolic pressure equilibration

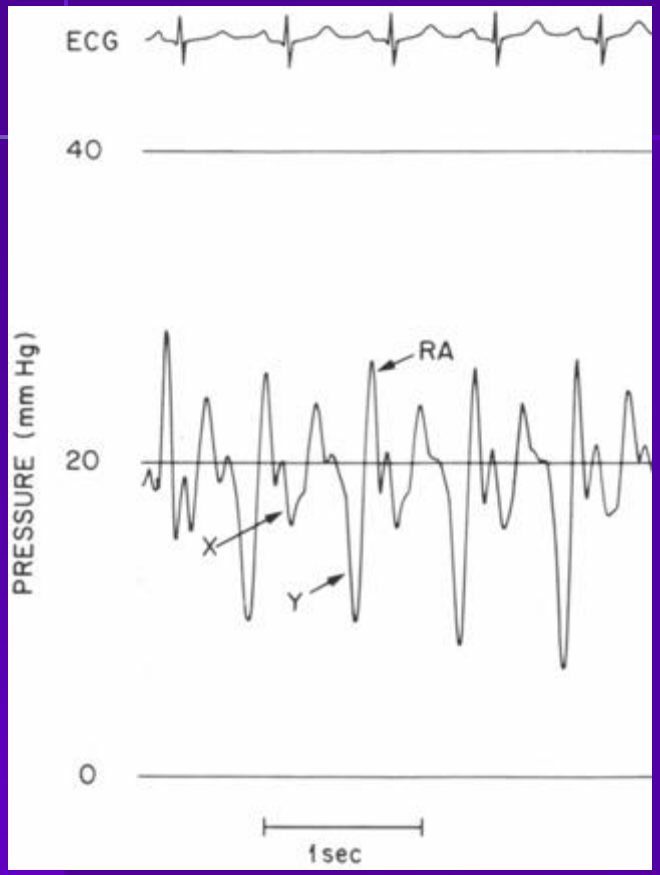
restrictive vs constrictive hemodynamics

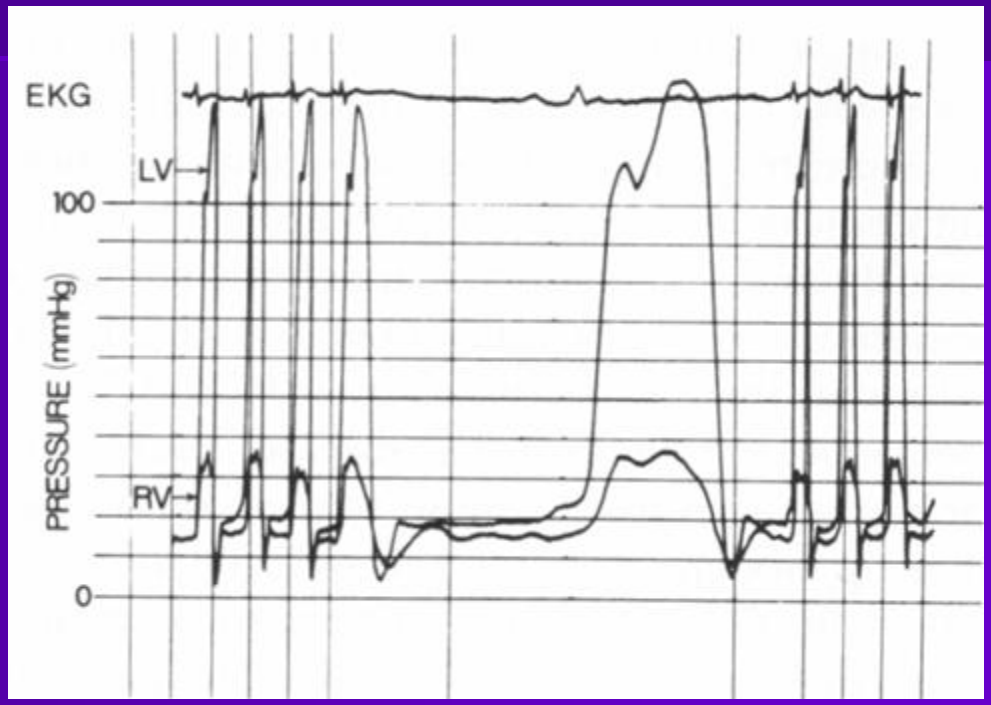
Endomyocardial biopsy-

definite Dx of restrictive pathology



Cardiac Catheterization





Prominent y descent — "dip and plateau"

rapid atrial emptying — rapid ventricular filling

then abrupt cessation of blood flow due to non-compliant myocardium

Constriction vs. Restrictive CM

TABLE 2. THE DIFFERENTIAL DIAGNOSIS OF RESTRICTIVE CARDIOMYOPATHY AND CONSTRICTIVE PERICARDITIS.*

TYPE OF EVALUATION	RESTRICTIVE CARDIOMYOPATHY	CONSTRICTIVE PERICARDITIS
Physical examination	Kussmaul's sign may be present Apical impulse may be prominent S3 may be present, rarely S4 Regurgitant murmurs common	Kussmaul's sign usually present Apical impulse usually not palpable Pericardial knock may be present Regurgitant murmurs uncommon
Electrocardiography	Low voltage (especially in amyloidosis), pseudoinfarction, left-axis deviation, atrial fibrillation, conduction disturbances common	Low voltage (<50 percent)
Echocardiography	Increased wall thickness (especially thickened interatrial septum in amyloidosis) Thickened cardiac valves (amyloidosis) Granular sparkling texture (amyloid)	Normal wall thickness Pericardial thickening may be seen Prominent early diastolic filling with abrupt displacement of interventricular septum
Doppler studies	Decreased RV and LV velocities with inspiration Inspiratory augmentation of hepatic-vein diastolic flow reversal Mitral and tricuspid regurgitation common	Increased RV systolic velocity and decreased LV systolic velocity with inspiration Expiratory augmentation of hepatic-vein diastolic flow reversal
Cardiac catheterization	LVEDP often >5 mm Hg greater than RVEDP, but may be identical	RVEDP and LVEDP usually equal RV systolic pressure <50 mm Hg RVEDP >one third of RV systolic pressure
Endomyocardial biopsy	May reveal specific cause of restrictive cardiomyopathy	May be normal or show nonspecific myocyte hypertrophy or myocardial fibrosis
CT/MRI	Pericardium usually normal	Pericardium may be thickened

*LV denotes left ventricular, RV right ventricular, LVEDP left ventricular end-diastolic pressure, RVEDP right ventricular end-diastolic pressure, CT computed tomography, and MRI magnetic resonance imaging.

Treatment

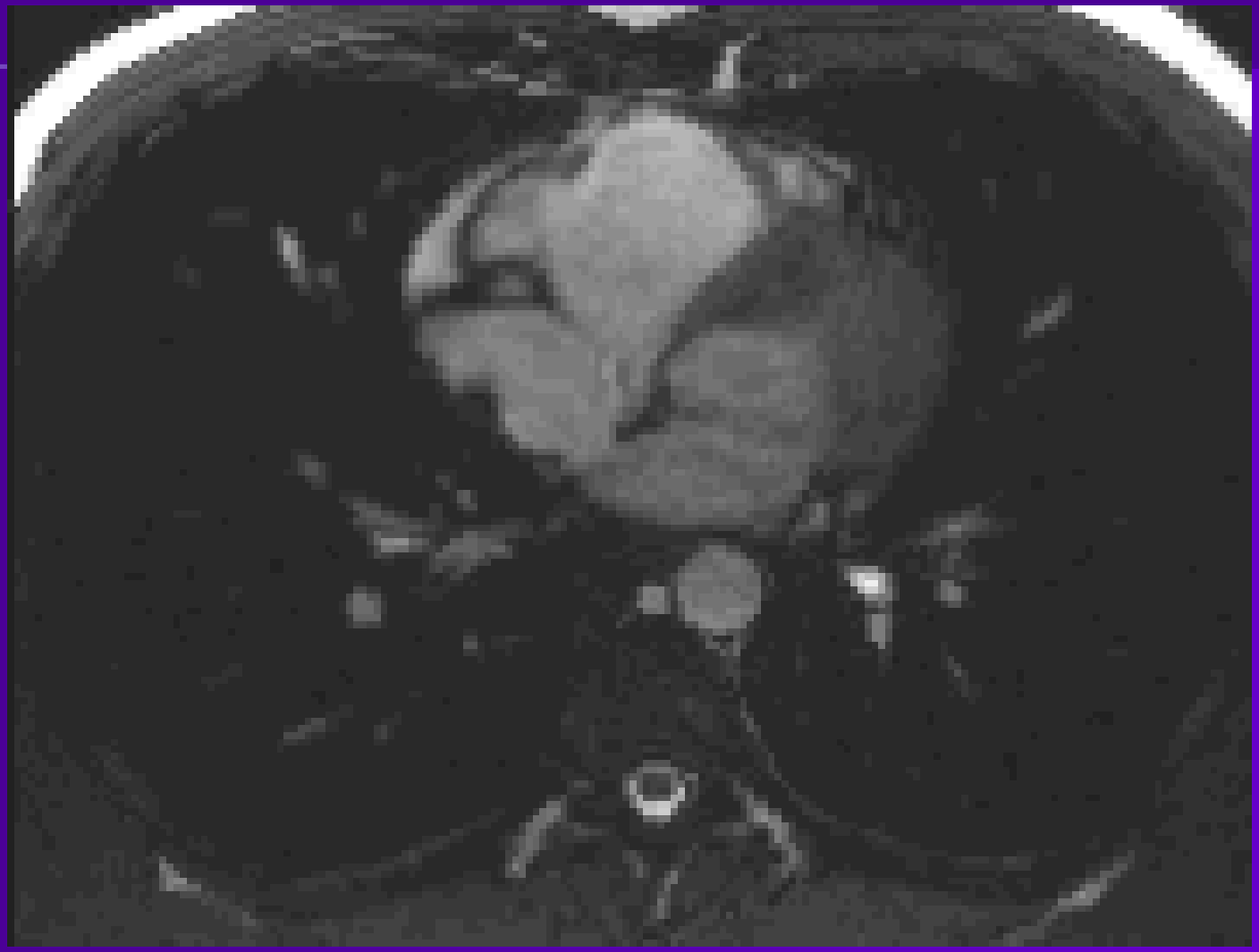
- Treat underlying cause
  - r/o constriction which is treatable (restriction poor prognosis)
  - amyloid (melphalan/prednisone/colchicine)
  - Endomyocardial Fibrosis (steroids, cytotoxic drugs, MVR)
  - Hemochromatosis (chelation, phlebotomy)
  - Sarcoidosis (steroids)
- Diuretics
  - For congestive symptoms, but $\downarrow$ LV/RV filling $\Rightarrow \downarrow$ CO
- Digoxin (avoid in amyloidosis)
- Antiarrhythmics for afib
  - amiodorone
- Pacemaker for conduction system disease
- Anticoagulation for thrombus (esp in atrial appendages)

What is the hemodynamic problem in RCM?

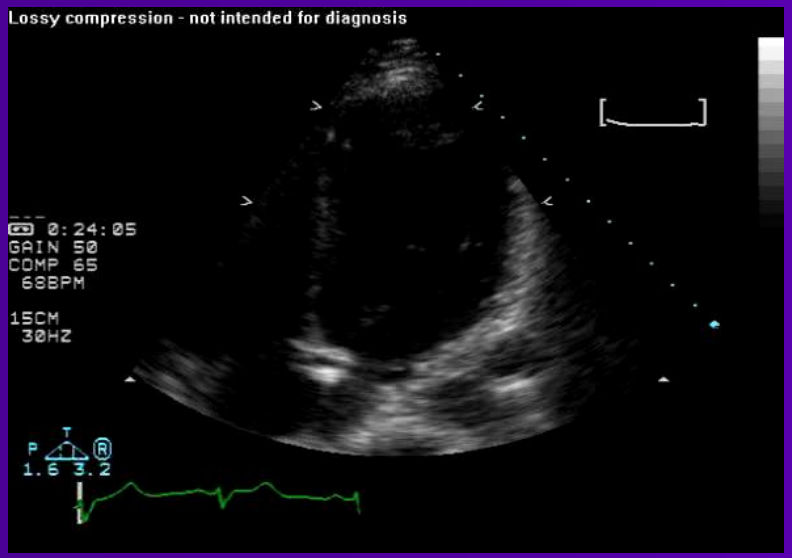
Arrhythmogenic RV Dysplasia

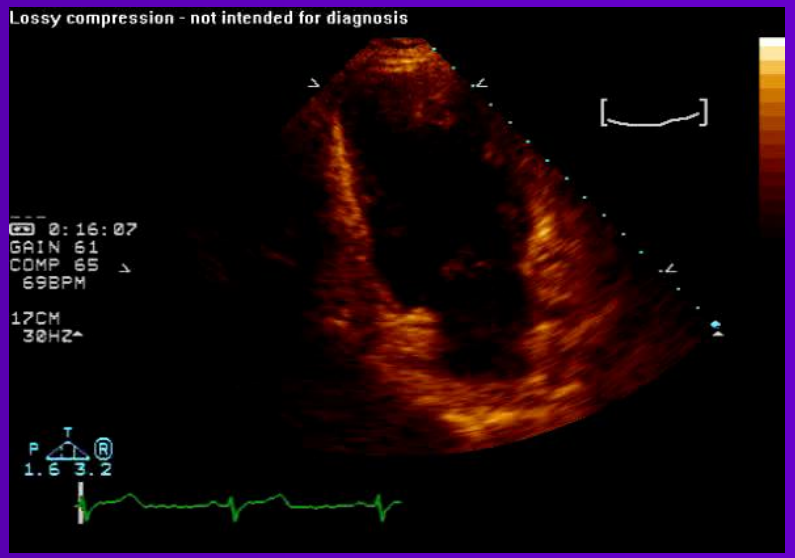
- Myocardium of RV free wall replaced:
  - Fibrofatty tissue
  - Regional wall motion/function is reduced
- Ventricular arrhythmias
  - SCD in young

MRI: RV Dysplasia



Echo: LV Noncompaction





LV Noncompaction

Diagnostic Criteria

- Prominent trabeculations, deep recesses in LV apex
- Thin compact epicardium, thickened endocardium
  - Stollberger C, JASE '04
- Other phenotypic findings

Prognosis and Treatment

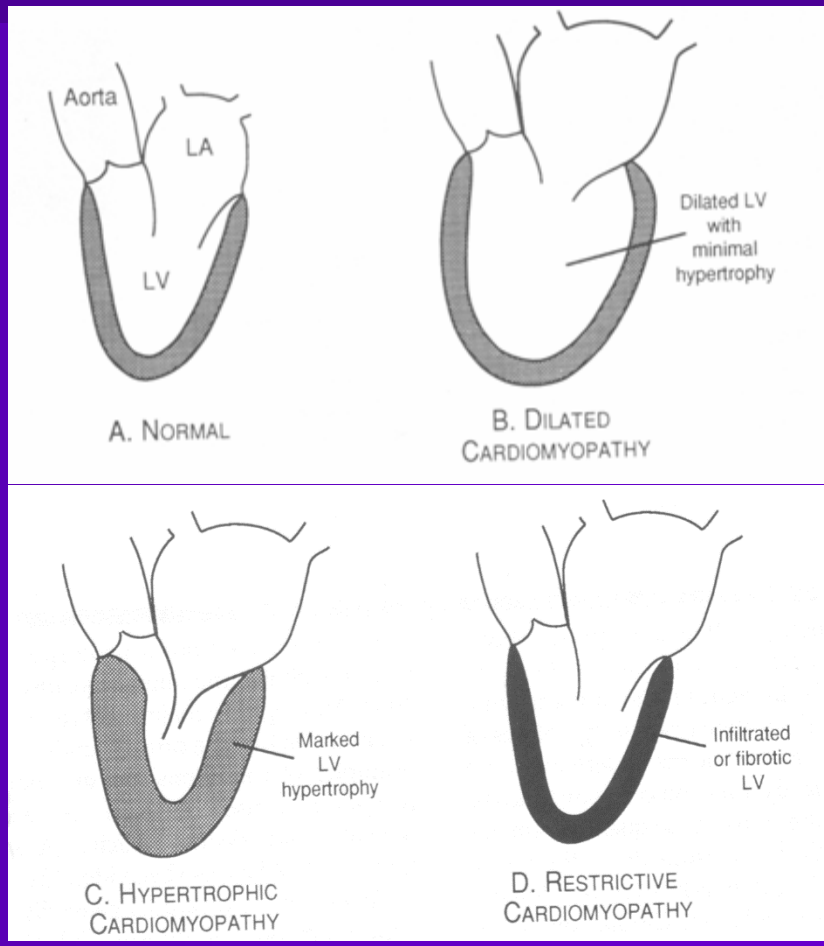
- Increased risk of CHF, VT/SCD, thrombosis
  - Oechslin EN, JACC '00
- Hereditary risk
  - Screening of offspring
- Pregnancy: case report

Cardiomyopathy

WHO Classification

anatomy & physiology of the LV

1. Dilated
   - Enlarged
   - Systolic dysfunction
2. Hypertrophic
   - Thickened
   - Diastolic dysfunction
3. Restrictive
   - Myocardial stiffness
   - Diastolic dysfunction
4. Arrhythmogenic RV dysplasia
   - Fibrofatty replacement
5. Unclassified
   - Fibroelastosis
   - LV noncompaction



Takotsubo-Like Left Ventricular Dysfunction

takotsubo fishing pot

left ventricular apical ballooning

www.grangeblanche.hautetfort.com

Why is Stress Cardiomyopathy Important?

- Mimics myocardial infarction
- Differentiate from grief response
- Educate patients on favorable prognosis
- Protect patients from exposure to unnecessary treatments

Stress Cardiomyopathy vs. Myocardial Infarction

Stress Cardiomyopathy

- Normal coronary arteries, no blockage
- Results in stunning of cardiac muscle
- Reversible condition

Myocardial Infarction

- Caused by blockages in coronary arteries
- Results in death of cardiac muscle
- Permanent, irreversible damage

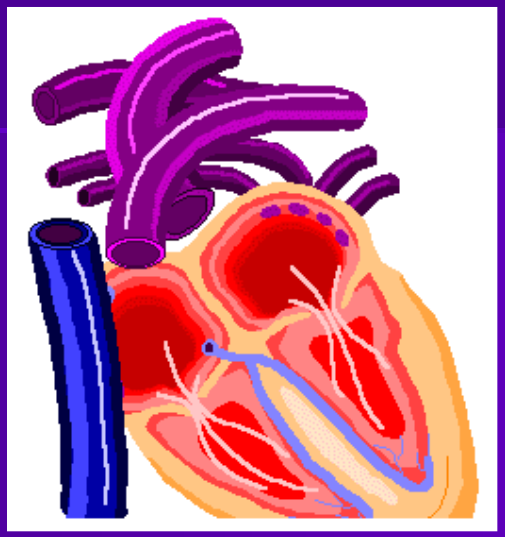
Possible Causes of Stress Cardiomyopathy?

- Catecholamine excess?
- Lack of estrogen?
- Or both?

Diagnostic Criteria Proposed by The Mayo Clinic

1. Transient loss or decreased movement of the left ventricular apical and mid-ventricular segments with regional wall-motion abnormalities extending beyond a single region supplied by a coronary vessel
2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture
3. New EKG abnormalities - either ST-segment elevation or T-wave inversion
4. Absence of recent significant head trauma, intracranial bleeding, pheochromocytoma, obstructive epicardial coronary artery disease, myocarditis, and hypertrophic cardiomyopathy

Decreased Left Ventricular Function



- Ejection fraction in healthy individual
  - >0.55
- Average ejection fraction at presentation
  - 0.39 - 0.49
- Average ejection fraction at follow-up
  - 0.60-0.79

Treatment Modalities

- Alpha Blockers
  - Help small blood vessels remain open
- Beta Blockers
  - Reduce catecholamine effects
- Short-term Anticoagulants
  - Prevent thrombus formation until function improves
- Supportive Treatment
  - ACE inhibitor, aspirin, IV diuretics
- Contraindications
  - Synthetic catecholamines
  - Thrombolysis in ST-segment elevation
  - ACE inhibitors in increased pressure gradients

The Future of Stress Cardiomyopathy

- Importance of ESTROGEN in stress response
- Identifiable DIAGNOSTIC measures
- RECOGNITION in medical community
- More EDUCATION about differences of cardiac symptoms in women vs. men

The Take Home Message

- Primarily affects postmenopausal females
- Often precipitated by severe stress
- Severe reversible left ventricular dysfunction
- Mimics myocardial infarction
- Increased catecholamines and lack of estrogen thought to play a role
- Alpha and beta blockers the best treatment